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TREATMENT OF RETINAL GLIOMAS BY THE FRACTIONATED OR DIVIDED DOSE PRINCIPLE OF ROENTGEN RADIATION

A PRELIMINARY REPORT

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If radiation therapy could be so administered as to destroy or control retinal glioma without undue injury to the function of the eye, there could be no question as to the superiority of this method over surgical removal of the involved eye, but a review of the literature will reveal that up to this time radiation therapy has met with little success in the treatment of this disease. Enucleation of one eye for unilateral glioma has been reasonably successful and is justifiable as a life-saving measure. Should the remaining eye show later involvement, or should bilateral involvement be evident from the beginning, enucleation of both eyes and total blinding of the child, even as a life-saving measure, would in the average case be so repugnant both to the physician and the parents as to make the natural course of the disease preferable, despite the blindness and death which would inevitably occur except in those very rare instances of spontaneous regression.

At the Memorial Hospital for the Treatment of Cancer and Allied Diseases (hereafter referred to as the Memorial Hospital) may be found the records of forty-four cases of retinal glioma. A patient with this condition treated there by Drs. H. H. Janeway and Douglas Quick in 1917 has been made the subject of a report by Dr. Mark Schoenberg,[1]

This paper was read before the regular meeting of the Section of Ophthalmology of the New York Academy of Medicine on Dec. 16, 1935.

1. Schoenberg, M. J.: A Case of Bilateral Glioma of the Retina Apparently Arrested in the Non-Enucleated Eye by Radium Treatment, Arch. Ophth. **56**:221-228, 1927.

to which we shall again refer. Some of the patients were referred for prophylactic irradiation of the orbital cavity after enucleation of one eye. Others were treated by irradiation for local recurrence after enucleation, and a few were given radiation as a primary treatment. With the exception of the case observed by Janeway and Quick (reported by Schoenberg) and our present series, radiation therapy at the Memorial Hospital has not been successful in controlling demonstrable disease with conservation of the eye.

The series presented in this report was begun in February 1933 and consists of six consecutive cases of bilateral glioma in which treatment was by roentgen radiation in multiple divided doses through small portals over a period of several months. In four of the patients one eye had been enucleated before we began treatment. In one patient we removed one eye after four months of treatment because of atrophy of a buphthalmic globe, and in another we are irradiating both eyes at the present time (December 1935). The technic of irradiation of the gliomas in these patients differs markedly from any previously used in the treatment of retinal glioma and is based on the biologic principle developed by Coutard in the treatment of pharyngeal cancer.

None of the patients in our present series has as yet passed the five year period of freedom from active disease. In the first two cases of our present series we have obtained satisfactory results, in one after two years and ten months and in the other after two years and three months. The remaining four are all of shorter duration and the patients are progressing favorably under active treatment. So far, the treatment has failed in none of our cases.[1a] Our justification for making this preliminary report is that we believe that the method which we now employ has been more successful than any other heretofore reported. We have had proof of the existence of gliomas in five of our patients by histologic examination of the excised eye. In the sixth patient, in whom we have only ophthalmoscopic evidence, we are irradiating both eyes for bilateral glioma. The patients have been examined ophthalmoscopically under general anesthesia at about monthly intervals.

So far we have not recommended irradiation as the primary treatment for unilateral glioma, but our results to date have encouraged us in the hope that radiation may eventually supplant surgery in the treatment of all except advanced, complicated growths and that it may safely permit the retention of the affected eye with useful function.

Retinal glioma is a local disease, which usually progresses only by extension within the globe and along the course of the optic nerve;

1a. Since the original presentation of this paper glaucoma has developed in cases 3 (A. G.) and 4 (E. A.), and the patients are now under treatment for that condition. In case 5 (B. L.) recurrence has developed. In cases 1 (H. F.), 2 (L. C.) and 6 (R. O.) the patient is free from disease.

metastases seldom occur. Therefore the efficacy of any therapeutic method may be accurately measured by the character and permanency of the local result.

REVIEW OF REPORTED CASES IN WHICH TREATMENT WAS BY RADIATION

Radiation therapy has been employed in the treatment of retinal glioma for many years, and the literature published prior to 1920 contains numerous reports of such treatment.[2] Most of these reports concern single cases and describe the method of the irradiation vaguely; an occasional one gives the condition of the patient a few months to a year after the beginning of treatment. With the exception of those to be given presently there are no subsequent reports of the final condition of these patients, and we may fairly assume that in all of them the treatment eventually was a failure. We must commend the scientific integrity of Jaensch,[3] who in 1930 published a final report of three cases in which he had previously considered that cures had been obtained by radiation therapy. In this final communication he regretted to state that all three patients had died of the disease.

We have found reports of two five year cures—that obtained by Janeway and Quick (Schoenberg [1]) and another by Knapp and Lüdin.[4] Single three year cures have been reported by Moore,[5] Verhoeff [6] and Fleischer.[7]

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2. The first recorded case in which retinal glioma was treated by roentgen radiation was reported by Hilgartner (Report of a Case of Double Glioma Treated with X-Ray, Texas M. J. **18**:322-323, 1903). The patient had bilateral involvement and was given daily treatments with roentgen rays for a period of eighty-four days. The face was protected by a lead shield perforated for both eyes. At the completion of this treatment "careful examination revealed entire absence of any growth in the left eye and the right had shrunken to two-thirds its normal size." As might be expected from a report of over thirty years ago, the physical factors of the roentgen irradiation are omitted except for the treatment time, so that it is impossible to estimate the dose. From the text, we may infer that Hilgartner intended to publish a later report as to the result of the treatment. Since this was not done, we may fairly assume an eventual failure. The report is of particular interest to us in that Hilgartner in 1903 employed the principle of protracted irradiation with daily doses over a period of about three months.

3. Jaensch, P. A.: Die Prognose der Enukleation beim Melanosarkom der Uvea, Klin. Monatsbl. f. Augenh. **84**:649-662, 1930.

4. Knapp, P., and Lüdin, M.: Heilung eines Netzhautglioms durch Strahlenbehandlung, Klin. Monatsbl. f. Augenh. **83**:279, 1929.

5. Moore, R. F.; Stallard, H. B., and Milner, J. G.: Retinal Gliomata Treated by Radon Seeds, Brit. J. Ophth. **15**:673-696, 1931.

6. Verhoeff, F. H.: Glioma Retinae Treated by X-Rays with Apparent Destruction of the Tumor and Preservation of Normal Vision, Arch. Ophth. **50**:450-456, 1921.

7. Fleischer, B.: Bericht über den Verlauf des vor zwei Jahren vorgestellten Falles von Gliombestrahlung, Klin. Monatsbl. f. Augenh. **83**:332-334, 1929.

We have carefully examined and considered the irradiation technics as described in these five reports and have come to the conclusion that with the exception of two (that of Moore and that of Knapp and Lüdin) the dose of radiation reaching the tumor was so small that the favorable result must have been due to the unusual radiosensitivity and character of the individual tumor or to spontaneous regression rather than to the merits of the technic employed. Spontaneous regression of retinal glioma, generally considered as a rare phenomenon, is well authenticated, and the number of recorded instances is several times that of the reported cures by radiation.[8] The possibility of spontaneous

8. At least seven well authenticated cases of retinal glioma in which cure was spontaneous have been reported in the literature (Meller, J.: On the Retrogression of Retinal Glioma, Am. J. Ophth. **32**:193-199, 1915. von Hippel, E.: Selbstheilung eines Netzhautgliomas, Klin. Monatsbl. f. Augenh. **80**:30-32, 1928. Siegrist, A.: Gutartiges Glioma Retinae, ibid. **65**:387, 1920. Purtscher, O.: Zur Kenntnis des Markschwamms der Netzhaut und seiner spontanen Rückbildung, Centralbl. f. prakt. Augenh. **39**:193-206, 1915. de Kleijn, A.: Ueber die Frage der Spontanheilung bei Gliomata Retinae, Arch. f. Ophth. **80**:371-378, 1911. Lindenfeld, B.: Ueber Spontanheilung von Glioma Retinae, ibid. **86**:141-144, 1913. Knieper, C.: Ein Fall von doppelseitigem Glioma Retinae, ibid. **78**:310, 1911). The final reports on all of these have been given after follow-up periods of from eight to thirteen years. In all except von Hippel's case the diagnosis was established microscopically in one eye. There are other instances in which regression was spontaneous with a resumption of growth at another site after a year or so (Deutschmann, F.: Ueber ein atypisches Netzhautgliom, Ztschr. f. Augenh. **27**: 225-235, 1912. Axenfeld, T.: Weitere Erfahrungen mit intraokulärer Strahlentherapie, Ber. u. d. Versamml. d. deutsch. ophth. Gesellsch. 1918, p. 312. Wintersteiner, H.: Das Neuro-epithelioma retinæ: Eine anatomische und klinische Studie, Leipzig, 1897). Of the seven reported cases in which cure was spontaneous, the eye had good function in four (Meller, von Hippel, Siegrist, Purtscher), while in three the regression (de Kleijn, Lindenfeld and Knieper) resulted in phthisis bulbi. The ophthalmoscopic appearance of the arrested lesions in the functioning eyes seems to have been identical with that in the arrested processes which we observed in our cases 1 and 2. Von Hippel gives a drawing of the lesion of the fundus in his case, and it appears similar to that in our case 2. Meller, in describing the ophthalmoscopic appearance in his case, spoke of the tumor as being composed of "crumby, chalk-like white masses" surrounded by a pigmentary disturbance. He has unquestionably described here the unabsorbed, residual calcium content of the lesion. The descriptions of the microscopic appearances in the enucleated phthisical eyes all mention the calcium and bone content. Apparently the findings in these phthisical eyes were identical with those which we noted in the eye which became atrophic (case 4) in the course of the tumor's regression following irradiation. The only differences were those that time alone would make, i. e., bone formation and further organization leading to phthisis bulbi. These advanced degenerative changes in the globe were particularly noted in the case reported by Knieper. Here the one eye was enucleated and the diagnosis of retinal glioma established. A short time later the other eye was completely filled with glioma and the globe was buphthalmic. The parents refused enucleation of the second eye, and the child was sent away to die. In following up their cases of glioma, eleven years later a letter was sent to the local doctor to find out how long this patient

(Footnote continued on next page)

healing must therefore be considered in connection with any instance of a cure by radiation, our own included. The merit of any particular method of treatment is determined by the consistency of the results rather than by the apparent result in any single instance.

In most classes of comparatively radioresistant tumors there will occasionally be found an isolated instance of marked radiosensitivity, as evidenced by complete regression under small or moderate dosage. Emotional or specious reasoning may lead to self-deception and unjustified optimism in regard to the merits of the technic employed, which may have failed consistently in the past and which may prove unavailing in the future. We have endeavored to avoid such errors in presenting this report.

A retinal glioma showing marked radiosensitivity must be considered as a rare exception, and a plan of irradiation based on observation of exceptions will be found to be of little practical value in the management of the majority of retinal gliomas since, in our experience, most retinal gliomas prove to be radioresistant.

The first five year cure recorded in the literature was that in a patient treated at the Memorial Hospital in 1917 by the late Dr. H. H. Janeway and Dr. Douglas Quick and reported by Dr. Mark Schoenberg [1] in 1927. We have examined the original record with the following findings: The first treatment was given in 1917 by Dr. Janeway and consisted in the application to the temporal region of 144 millicurie hours with a filter of 0.5 mm. of lead. The distance and the radiating area of this application are not given, but, however it was placed, one can be certain from an elementary knowledge of the physics and biologic effects of radiation that less than one-quarter skin erythema dose was delivered to the tumor. Five months later a second treatment was given by Dr. Janeway, consisting in the application of 460 millicurie hours over an area of 4 sq. cm. at a distance of 1 cm. with a filter of 2 mm. of lead. This application would have delivered between 2 and 3 skin erythema doses to the skin (distance, 1 cm.) but only from one-sixth to one-tenth skin erythema dose to the tumor (distance, from 3 to 4 cm.).

In his report of the ophthalmoscopic examination of the eye two months later Dr. Janeway states that "the tumor was unchanged in appearance," which was to be expected since the growth had received an insignificant total dose. A third dose of radiation was given by Dr.

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had survived. Much to Knieper's surprise, he was informed by the local doctor that the patient was well and living in an institute for the blind. The patient was visited; the remaining eye had become phthisical, and permission for enucleation was obtained. Microscopic examination showed no evidence of the tumor but only far advanced degenerative changes with a great deal of calcium and bone. The retinal and choroidal elements were not recognizable.

Quick in 1918 with the "lead tray," consisting of 3,000 milligram hours with a radiating surface of 20 sq. cm., a distance of 3 cm. and a filter of 2 mm. of lead and 0.5 mm. of silver. This application would have delivered about 1 skin erythema dose to the skin of the eyelids, but at the level of the retina the dose would have been less than one half of that. From personal experience we feel safe in stating that the cure in this case was due to the unusual character and radiosensitivity of this particular tumor, rather than to the quantity of treatment given. If glioma could be made to regress with such tissue doses, there would be no difficulty in administering it in every case and the control of this disease would be a simple problem. In this patient a cataract subsequently developed, which was operated on some years later by Dr. Schoenberg, and we have learned in a recent personal communication that the patient survives with fair vision in the affected eye, eighteen years after treatment.

Knapp and Lüdin [4] in 1929 reported a five year cure of a glioma treated in 1923 and 1924. Their published description of the physical factors of the irradiation is incomplete, so that it is not possible to determine even the approximate quantity of radiation delivered to the tumor.[9] Six radium treatments were given externally to the eye between January and March 1923, the dose at each treatment varying from 40 to 120 milligram hours, but the distance and the character of the filter are not specified. Several months later they began giving a series of roentgen treatments, and in the following two years eleven applications were made over the eye. The factors of the roentgen treatments are not completely given, so that it is impossible to state the exact dose. Five years later the patient was operated on for cataract, at which time the retina was carefully examined and found to be free from disease. The six radium treatments over a period of several months totaled about 500 milligram hours, and this dose, no matter how applied externally, would produce less than 1 skin erythema dose in the tumor, even if given at one time rather than over a long period. (Compare this dose with

9. The physical factors which must be specified in order to describe adequately the dosage of radium and of roentgen rays are as follows:

For roentgen rays: (1) the kilovoltage, (2) the milliamperage, (3) the target skin distance, (4) the thickness and character of the filter, (5) the size of the skin portal and (6) the duration of the exposure. If the tissue dosage is to be discussed, the depth of the lesion should also be stated. Recently the term "roentgen" ("r") has been applied in designating the measurement of roentgen radiation. The total r can be substituted for milliamperage and time; all other factors must be specified.

For radium radiations: (1) the radium or radon content, (2) the area of radiating surface, (3) the distance, (4) the thickness and character of the filter and (5) the time of application. Usually the product of 1 and 5 is added under the term "milligram hours" or "millicurie hours."

that given by Dr. Janeway in the preceding case.) It is possible that the eleven roentgen treatments given over the period of the succeeding two years delivered a tissue dose capable of bringing on regression in a radiosensitive tumor, but since the factors of the irradiation are incompletely reported one can gain little practical information from this report.

The three year cure reported by Moore [5] and co-workers was obtained by twice suturing filtered radon seeds in doses of 5.3 and 12 millicuries, respectively, to the sclera directly over the tumor. The quantity of radiation delivered to the tumor with these applications was in the neighborhood of 5 to 10 skin erythema doses. (It is not possible to give a more exact approximation without knowing the exact size of the tumor and the arrangement of the seeds.) Three years later the growth had shrunk down to an irregular scarred area and appeared stationary, with satisfactory vision in the eye. The probable tissue dose delivered to this tumor would be adequate to control even a radioresistant tumor, and the result obtained was in all likelihood due to the treatment given. In the same report, however, these authors cite four other attempts to cure glioma by the same method, which were failures. In our opinion, the technical difficulties of interstitial implantation of radon in retinal gliomas and the attendant complications are serious disadvantages of this method.

Verhoeff's [6] patient, who also had a three year result, received a "suberythema dose" of lightly filtered roentgen radiation to the eye once a week for three weeks. Meller [10] reported a case of his own as one in which spontaneous regression took place, despite the fact that two small doses of roentgen radiation had been given. He compares his case with Verhoeff's and is of the opinion that in both cases the cures were spontaneous. Fleischer's [7] patient with a three year result was treated with four doses, each 70 per cent of a skin erythema dose, at intervals of three months. In our opinion, any one familiar with the biologic effects of radiation will suspect that both the latter cures were spontaneous regressions rather than effects of radiation, since the doses delivered to the tumors were comparatively insignificant.

With the exception of that obtained by Moore (and possibly that obtained by Knapp and Lüdin) the reported cures depended on the use of such small doses of radiation that critical analysis and judgment force one to the conclusion that none of the technics and radiation dosages described may be used as models for the future treatment of glioma. The most striking similarity is that the doses delivered to the tumors were small. After these single successes, the same authors

10. Meller, J.: Ueber spontane Heilung von Netzhaut Gliom, Ztschr. f. Augenh. 49:1-4, 1922-1923.

undoubtedly applied the same technic in other cases, but they reported no further cures. If permanent cures could be obtained consistently by such technics and dosages, the successful treatment of glioma by radiation would be a simple matter, since it could be carried out with about the same technic and dosage used by dermatologists in the treatment of dermatoses of the skin. If in the treatment of any disease the successful therapeutic result obtained in a single instance by a particular method cannot be consistently repeated, the report of a successful cure is interesting only as a medical curiosity.

GENERAL PRINCIPLES FOLLOWED IN TREATMENT

The technic of treatment and the dosage of radiation employed in our present series differ markedly from any previously reported for the treatment of glioma. The most important factors may be enumerated as follows:

1. Multiple small portals 2.5 cm. in diameter
2. Accurate direction of the beam of roentgen radiation
3. Multiple treatments, from 50 to 75
4. A long period of treatment, up to twenty months

We have planned our technic with the conviction that retinal glioma is a radioresistant neoplasm which cannot be controlled by moderate dosage except in rare instances. Although the eye itself is fairly tolerant to radiation, we have felt that in order to retain a reasonable amount of function in the organ every possible precaution should be taken to protect the lens and the conjunctiva from untoward effects of radiation. The treatment has in all cases extended over a period of from six to fourteen months, during which time, through several small portals, we have given the largest possible quantity of radiation to the eye which was compatible with fair comfort and the integrity of the normal structures. The treatment has produced blistering of the skin exposed to the direct beam in all cases. If at any time the superficial (skin) effects of the radiation became too pronounced in the eyelids, conjunctivae and corneas, with photophobia and tearing of the eyes and irritablity of the child, we usually gave the patient a month's rest until these effects and symptoms had subsided, and then recommenced the treatment with radiation. In the average case, the applications have been given at the rate of about two or three a week, the single doses varying from 250 to 400 r. The two patients who have completed treatment received seventy-three and forty-six exposures, respectively.

TECHNIC

Physical Factors of the Roentgen Radiation.—We have employed roentgen rays at 200 kilovolts and 30 milliamperes, with a filter of 0.5 mm. of copper and

2 mm. of aluminum, a distance of 65 cm., circular portals 2.5 cm. in diameter and an intensity of about 35 r per minute. The physical factors of the radiation are the same as those generally used at the Memorial Hospital for high voltage therapy, with the exception of the small circular portals 2.5 cm. in diameter. This and a few other phases of our technic merit a more detailed discussion.

1. *Size, Shape, Number and Location of the Skin Portals.*—In the intensity necessary for the control of glioma all radiation which strikes the uninvolved portions of the eye or surrounding structures is not only useless but distinctly harmful, and therefore, if one is to deliver an adequate dose to the growth safely, it is essential that the beam of roentgen rays be confined so far as possible to the immediate area of the tumor. We have considered that this end is best accomplished by the use of small circular portals (2.5 cm. in diameter), which we obtain by using a metal cylinder to confine the beam and permit it to be aimed at the posterior wall of the globe, much as one sights along the barrel of a rifle at a small target.

From the practical standpoint, we have found that the posterior wall of the globe may be irradiated from only three cutaneous portals or positions, as illustrated in figure 1 *A, B* and *C*. These may be described as follows: (1) temporal portal, just lateral to the outer canthus; (2) nasal portal, on the opposite side of the bridge of the nose, the beam being pointed contralaterally and slightly backward; (3) eye direct, the beam being pointed directly backward through the pupil of the eye.

2. *Maintaining the Orbit in Its Correct Relation to the Fixed and Limited Beam of Roentgen Rays During Treatment.*—This is an extremely important and rather difficult task, which may require both patience and tact. Small errors in the direction of the narrow beam are of sufficient significance to determine the difference between success and failure. By sighting along the cylinder, the beam of radiation is aimed at the posterior wall of the globe, and the child's head is held in direct contact with the cylinder during treatment. Often it will be found advantageous to mark the position of the cylinder on the skin with ink.

Up to the age of 5 or 6 years, the child cannot be expected to cooperate, and some one must hold its head firmly in the proper position. This task we have felt to be the duty of the parents or other members of the family because of the slight danger of general exposure to roentgen rays and also because the duty of repeatedly holding a crying struggling baby in a fixed position for ten minutes at each treatment is rather onerous. By patiently explaining the importance of this duty and the reasons for the parent's undertaking it, and by giving a simple description of the local anatomy in relation to the gliomatous mass, we have found that even the less intelligent parent will do his part quite acceptably. Ordinarily, one parent holds the child's head and the other the body, which is partly stabilized by pinning it inside a folded bedsheet. These positions and the locations of the portals are illustrated diagrammatically in figures 1 and 2.

3. *Size of the Individual Dose, Frequency of Treatments, Total Period of Treatment and Total Dose.*—These factors must be considered together since each one depends so much on all the others. The size of the individual dose has varied between 250 and 400 r and has depended somewhat on the frequency with which the single exposures were given. In deciding on the frequency of treatments, one must compromise to some extent between the probably ideal method of daily exposures and the nuisance and adverse effect on the child's health of daily trips to the clinic. We have found that both the patient and the parents are able to make about two or three visits per week over periods of several months. Giving two or three treatments a week, we have found that from 300 to 350 r per treat-

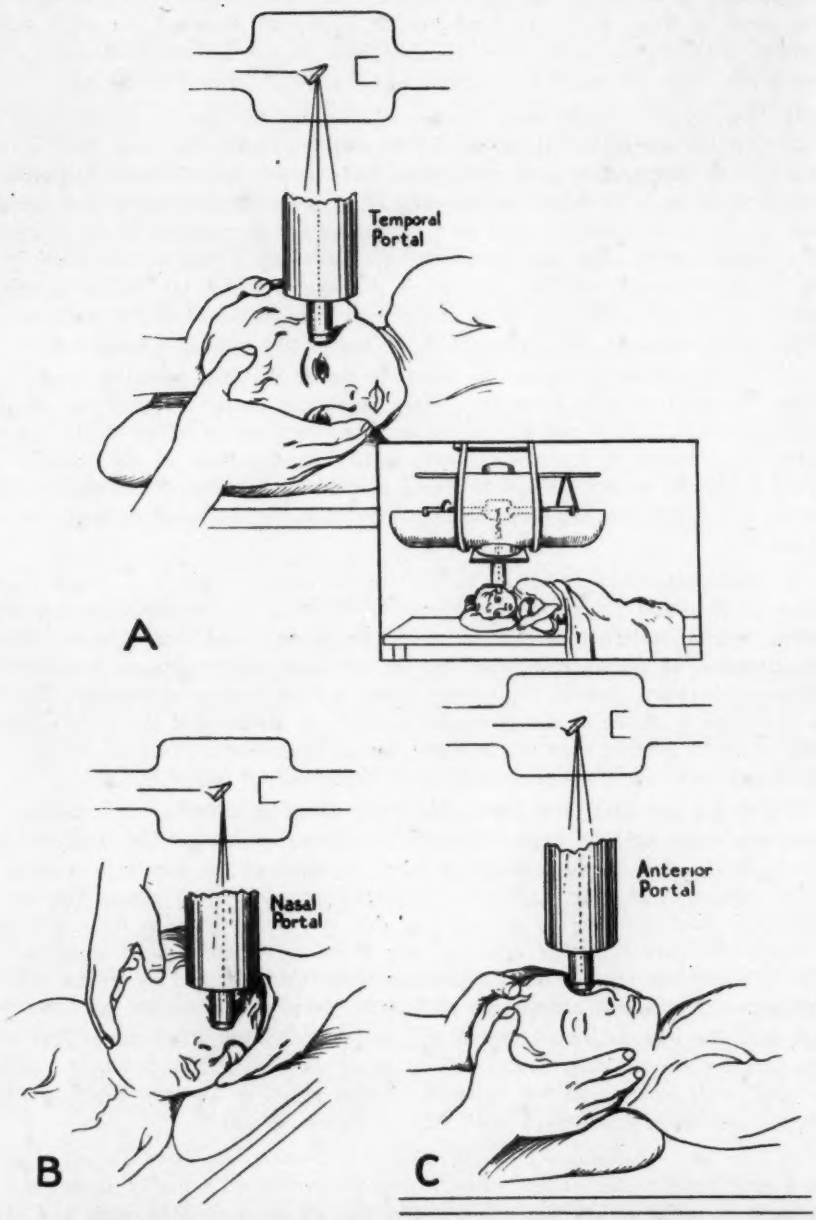

Fig. 1.—The application of roentgen radiation to retinal glioma by means of a metal cylinder which confines the beam and permits it to be aimed at the posterior wall of the ocular globe: *A*, temporal portal; *B*, nasal portal; *C*, anterior portal. The patient's head is held in contact with the cylinder of the x-ray machine by the parent or other relative, who is instructed how to hold the head so that the beam will be aimed at the posterior wall of the globe.

ment to one of the portals in rotation is about the optimum. Each portal therefore receives a treatment about every five to seven days. An individual dose of 250 r per treatment is rather less than can be tolerated, and with 400 r, the marked reaction in the skin and conjunctiva comes on earlier, so that it is too often necessary to interrupt the series in order to permit the reaction to subside. Usually we begin by including a direct portal to the eye as well, but after about 1,800 to 2,000 r the symptoms of photophobia come on, and we then discontinue the use of this anterior portal and proceed with the other two alone. These figures for dosage and this discussion apply only to circular portals 2.5 cm. in diameter. With portals of different sizes, a different set of figures for dosage would apply.

The total treatment has extended over variable periods up to twenty months, as shown in figure 3. We are not as yet certain what length of period for the total treatment will be productive of the best results. It will be noted that in our two oldest cases (1 and 2), in which also successful results were obtained,

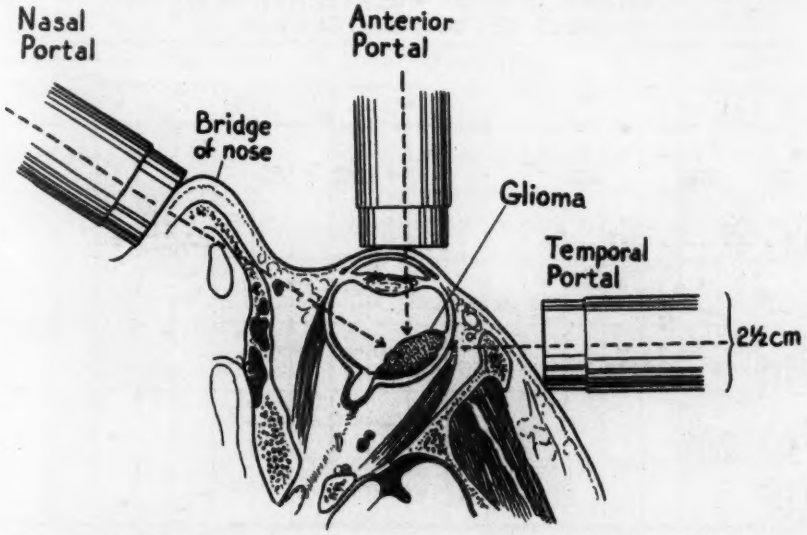

Fig. 2.—A cross-section diagram showing the path and objective of the roentgen rays as directed through each of the three portals in turn.

the periods for the total treatment were sixteen and twenty months, respectively. The intervals of rest were rather irregular and depended on whether the reaction in the eyelids and conjunctiva called for interruption of the treatment, and at other times treatment was resumed because ophthalmoscopic examination suggested some return of activity of the growth.

In general, we believe that the frequency of the treatments and the increase of the dose should be as fast and the total amount as great as is compatible with the comfort and health of the child and with preservation of the integrity and function of the eye and adnexa. Under such a plan the treatment will necessarily extend over a period of several months. One of our patients (case 5) has almost complete regression at this time, after five months and fifty-four treatments. This has been the most rapid regression in our experience. The total doses received by the individual skin portals are given in figure 3 and it will be seen that in case 2 the patient received 13,000 r to the temporal portal over a period of twenty months. The skin over that portal was blistered on two or three occasions but healed within

a few weeks after the treatment was interrupted. After the skin had healed, the treatment was resumed. Such large total doses in roentgens are meaningless unless considered in relation to the size of the portal, the size of the individual dose and the length of the period for the total treatment. The skin in both cases 1 and 2 is perfectly healed, soft and moist, and we anticipate no future difficulty with it. The conjunctivitis has cleared up in all cases, leaving a perfectly satisfactory end-result. The cilia sometimes drop out with the first marked reaction in the lids, but usually return.

CLINICAL COURSE

About every month throughout the course of the treatment each patient has been examined with the ophthalmoscope through dilated

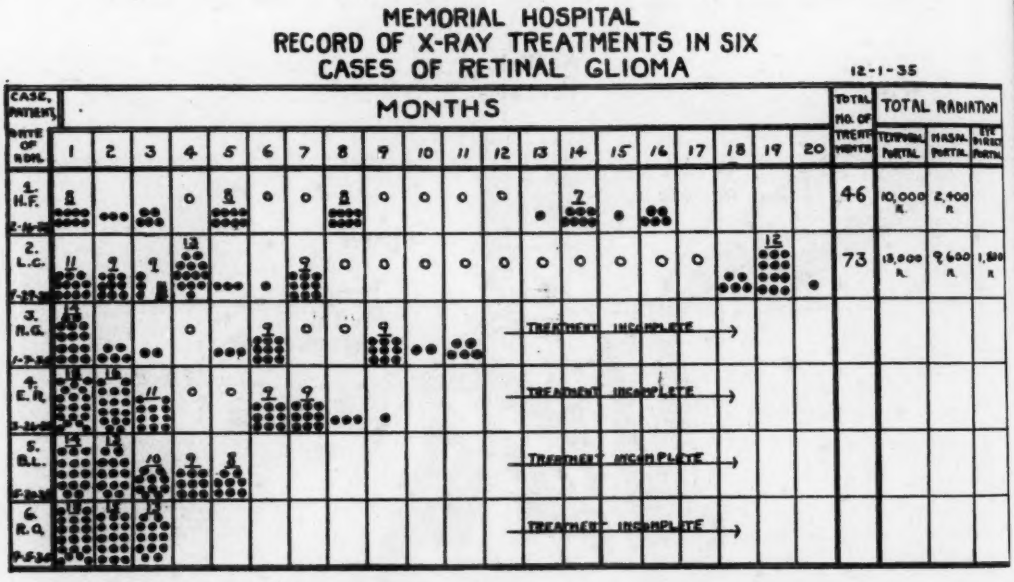

Fig. 3.—Record of roentgen treatments in six cases of retinal glioma.

pupils under chloroform anesthesia. To help compare the lesion from one time to another, we have made notes, diagrams and sketches at each examination.

1. *Cloudiness of the Retina Surrounding the Lesion.*—Within a week or two after the beginning of treatment we have noted in most cases a grayish to yellowish-white zone in the retina surrounding the lesion. We thought at first that this might be a flat detachment due to the accumulation of a subretinal transudate, but there was no predilection for the dependent part of the lesion, and further observations have indicated that this appearance was produced by edema of the retina adjacent to the tumor. This retinal edema was usually noted during active treatment, and it subsided when the treatment was less strenuous or soon after it was discontinued.

2. *Alteration in the Contour of the Lesion.*—This can be followed either by measurement with a grid projected in the ophthalmoscopic field or less accurately by estimation in disk diameters. After the first or second month we have commonly noted a recession of the border of the tumor. This has usually appeared first in the upper half, while the lower half seemed to be more sharply demarcated and in some instances overhanging. We have interpreted this as indicating sufficient dissolution of the tumor tissue to allow it to gravitate somewhat to the more dependent portion, thereby leaving a receded upper border and a sharper, somewhat pendulous lower border. Recession of the border has proceeded slowly for from four to eight months as the broken down tissue absorbed, with the regular contour noted in the lesion before the application of radiation becoming more or less irregular. The area over which the tumor has receded around the base has been outlined by a disturbance of the pigmented epithelium (figs. 7 *C* and 8 *B*). This area of pigmentary disturbance represents only the recession at the base of the lesion and is not an index of the recession which has taken place over the part of the tumor which protrudes into the vitreous. Nevertheless, the appearance of this pigment represents regression, and as such its accurate location and extent are considered important.

3. *Decrease in the Height of the Lesion.*—An attempt was made from time to time to estimate the height of the lesion in diopters. This did not prove to be a very satisfactory criterion, because the margin of error was too great in comparison with that which we were trying to measure. It may be said, however, that there was a decrease in the height of the lesion which was commensurate with the recession of its border. As the height decreased, the surface of the tumor became more irregular in contour.

4. *Vascularity.*—A decrease in the vascular channels over the surface of the lesion, other than those that normally occur in the retina, was noted in from two to four months. This vascularity should decrease gradually, and an increase at any area is the best index of the continuation or the resumption of growth. In two instances we noted an increase in the vascularity of the lesion at one site after the course of treatment was almost completed, and in both cases we resumed treatment.

5. *Calcification.*—In a nonirradiated retinal glioma, it is known that calcification frequently occurs. It is usually seen in the microscopic sections, and Pfeiffer [11] has demonstrated its presence by roentgenograms in 75 per cent of the cases which he has examined. Viewed with the ophthalmoscope it can often be seen over the surface of the lesion

11. Pfeiffer, R. L.: Roentgenographic Diagnosis of Retino-Blastoma, Arch. Ophth. **15**:811-821 (May) 1936.

as small irregular chalky to pearly white discrete and confluent areas, and its recognition is, in our opinion, pathognomonic of a retinal glioma in contrast with the various forms of pseudoglioma (fig. 4). In the microscopic sections of a retinal glioma the calcium is seen in the places where the tumor tissue has outgrown its blood supply and thereby become necrotic (fig. 5).

Fig. 4.—A drawing of the ophthalmoscopic appearance of a nonirradiated retinal glioma showing calcium foci at *a*.

The treatment of a retinal glioma with roentgen rays according to the method described here causes more necrosis of the tumor tissue and more precipitation of calcium. The irradiation, therefore, ultimately reduces the lesion to necrotic tissue and calcium (fig. 6). The former tends to absorb gradually while the latter persists. The end-stage then is a somewhat elevated chalky to pearly white avascular mass, composed mostly of calicum and surrounded by some pigmentary changes (figs.

7 C and *8 B*). The actual and relative increase in the calcium content of the lesion as observed ophthalmoscopically is the best index of regression.

6. *Vision.*—In both patients in whom the treatment has been completed there is no evidence of impaired retinal function. There must be a scotoma in the field of vision corresponding to the site of the lesion, although this has never been determined perimetrically, because of the age of these patients. The central vision in the first patient is 10/20 (pictures), and that in the second, 20/20. The latter patient is old enough to attend school, where he does satisfactory work with no apparent handicap. The vision of the other patients, in whom the treatment is incomplete, cannot be measured, because of their age.

COMPLICATIONS

Intra-Ocular Complications.—1. Hemorrhage: During the course of treatment small hemorrhages have been occasionally noted over the surface of the lesion. They were usually in an area where there was a considerable number of new-formed blood vessels. These hemorrhages have always absorbed, and they have never been large enough to enter the vitreous.

2. Detachment of the Retina: In a certain eye with multiple large retinal gliomas treated by a few massive doses at the Memorial Hospital some years ago, not included in the present series, a detachment of the retina developed following the disappearance of the tumor. This was due to the shortening of the retina through contracture of the scar tissue in it, which caused complete detachment from the optic nerve to the ora serrata. This retinal detachment, viewed ophthalmoscopically, gave a false appearance of progression of the tumor. We have so far not had such a complication in the series treated by the method described in this article.

3. Atrophy of the Globe: The fourth patient (E. A.) in our series had a bilateral glioma. The eye with the smaller lesion has responded satisfactorily to the radiation. The other eye contained a glioma so large that it seemed to fill the vitreous cavity. There were secondary glaucoma and buphthalmos. After from one to two months of treatment with radiation, blood appeared in the anterior chamber, and after three months the eye became atrophic and enucleation was performed. The tumor mass was so large that its dissolution and absorption were more than the eye could tolerate, and atrophy of the eyeball ensued. The microscopic examination showed no viable tumor tissue except for one small nest of cells in the choroid. The lesion had been reduced to necrotic tissue and calcium (fig. 6).

4. Cataracts: Cataracts have not developed in any of the patients, nor are there any signs of incipient changes now. Of course, sufficient time has not elapsed as yet to enable us to report fully on this feature.

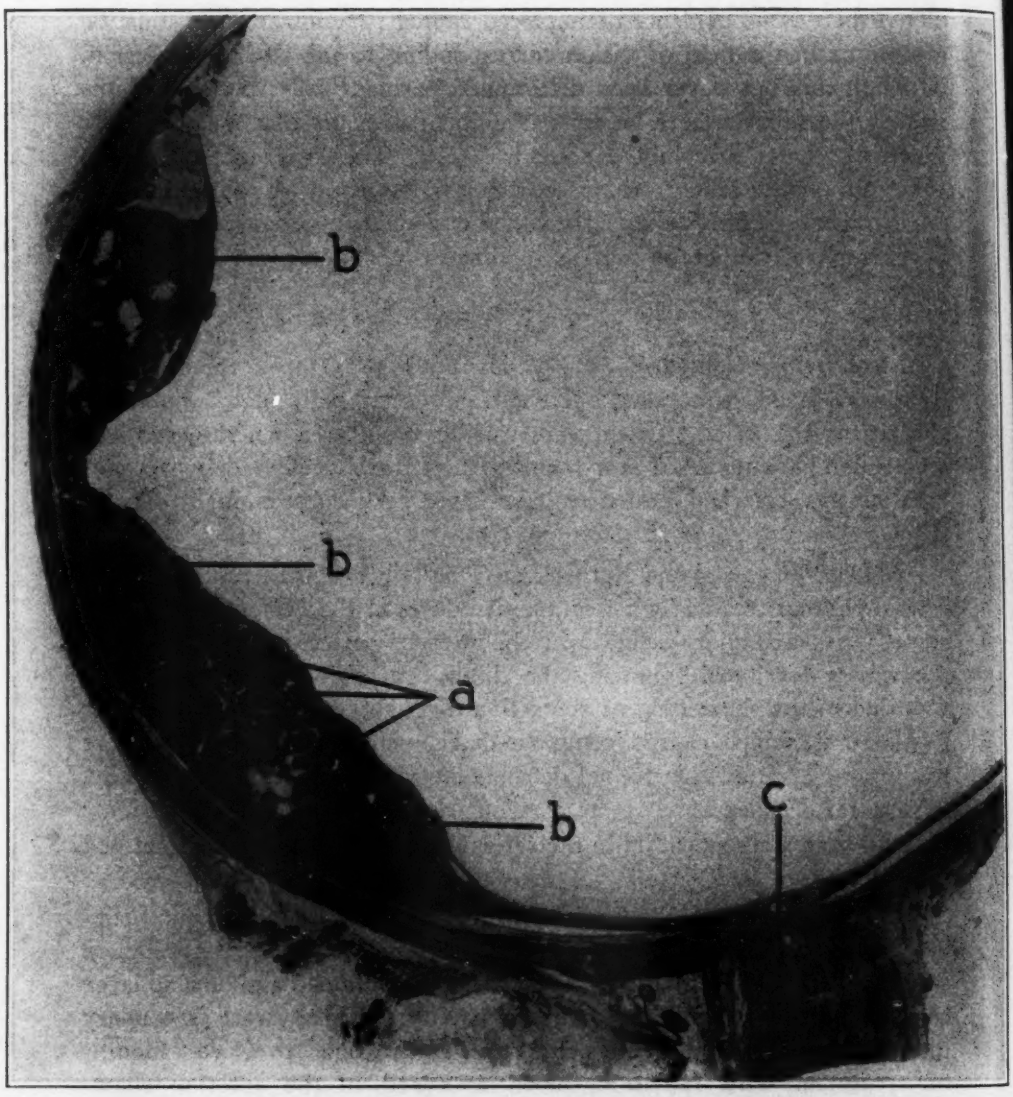

Fig. 5.—A microscopic cross-section of the eye the fundus of which is shown in figure 4: (*a*) the calcium foci seen ophthalmoscopically in figure 4; they are scattered through necrotic tumor tissue; (*b*) viable tumor tissue; (*c*) optic nerve.

Extra-Ocular Complications.—1. Early: Within from two to three weeks after irradiation was started, we noted erythema of the exposed skin, and sometimes after protracted treatment there was even purulent

dermatitis. The conjunctiva tolerates the radiation much better than the skin. When the conjunctiva was congested, this was usually due either to corneal involvement, which will be mentioned later, or to mucopurulent conjunctivitis secondary to the entrance of pus into the conjunctival sac from the adjacent radiodermatitis. After from one to two months of intensive treatment, one of the most annoying complications

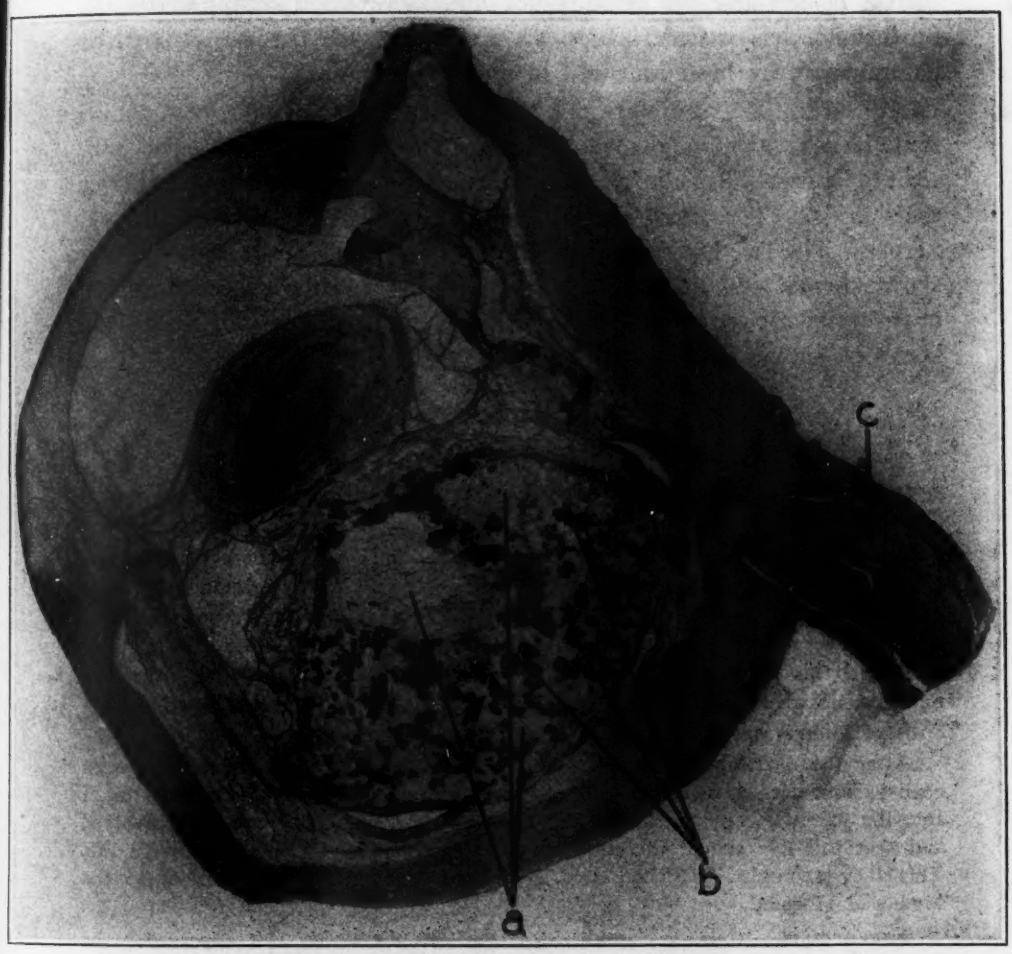

Fig. 6.—A microscopic section of the left eye of the patient E. A. (see text under "Atrophy of the Globe," p. 747). The vitreous cavity is partially filled with (*a*) necrotic tumor tissue, throughout which are scattered (*b*) innumerable foci of calcium. There has been some attempt at organization, which unites the necrotic lesion to the underlying choroid. No retinal elements are recognizable. At one site in the choroid there is a small nest of what seem to be viable tumor cells. This is apparently the only site of tumor tissue. There is no extension of the tumor cells into the optic nerve (*c*). The iris is completely necrotic and is represented by a small nub of fibrous tissue opposite the scleral spur. The lens is cataractous.

frequently arose in the cornea. There appeared a stippling of the corneal surface due to innumerable punctate areas which stained with fluorescein. The appearance was that of superficial punctate keratitis. This accounted for the photophobia and lacrimation which our patients showed when the treatment was intensive. When signs of this complication arose we usually discontinued treatment for a month, during which time the cornea healed and the photophobia and lacrimation disappeared. In no instance has vascularization or scarring of the cornea occurred or its transparency been impaired in any other way.

2. Late: The skin over the temporal portal has sometimes shown some bleaching and slight telangiectasis, but these changes are not sufficient to be a real blemish. No late skin changes have been noted at all over the eyelids. There was some dryness of the conjunctiva due to mild xerosis. The two patients in whom the treatment has been completed show no epilation of the brow or of the lashes, and there is no ectropion or trichiasis. Several of the patients whose treatment is incomplete, however, show some loss of lashes.

REPORT OF CASES

The first patient was referred by Dr. Ben Witt Key, who has made ophthalmoscopic examinations at regular intervals and has furnished us with the clinical observations.

CASE 1.—H. F., aged 9 months, was first seen by Dr. Key in February 1933. Her parents stated that when she was 6 weeks of age a white substance appeared in the pupil of the right eye, and on consulting an oculist they were informed that the eye should be removed as soon as possible. Three other consultations confirmed this opinion. Two weeks after the mass was first noted, when the infant was 8 weeks of age, the involved eye was removed. The preoperative diagnosis of glioma was confirmed histologically.

After the operation the condition of the remaining eye was observed by an oculist about once a month. Seven months later, when the child was 9 months of age, the parents were advised by the oculist that the left eye was also involved and that this eye should therefore be removed in order to save the child's life. This they refused. They consulted Dr. Key, who referred the patient to the Memorial Hospital.

Examination.—Right Eye: In February 1933, the right orbit appeared to be free from recurrence and the prosthesis well fitted.

Left Eye: There was no conjunctival or ciliary reaction. The iris was normal, and the pupil reacted to light and accommodation. The ophthalmoscopic examination revealed clear, transparent media. There was a fairly large typical glioma standing out in the vitreous, about 8 to 10 diopters in height. It occupied a large central area including the macula and the juxtapapillary region, extending to but apparently not involving the optic nerve. Another slightly elevated small round lesion was noted along the lower retinal vessels about 1½ disk diameters below the disk (fig. 7 *A*).

Treatment.—Between February 1933 and May 1934, the patient received forty-six roentgen treatments at the Memorial Hospital, the individual doses varying from 250 to 400 r, at the rate of two or three per week. The spacing of the treatments and the total period of the treatments are shown in figure 3.

Clinical Course.—After about six weeks of treatment the parents were of the opinion that there was definite improvement in the child's vision. Ophthalmoscopic examination under general anesthesia at this time revealed definite though slight reduction in the size and prominence of the tumor. The margins of the growth were thinner and the elevation undoubtedly reduced. The central portion was made

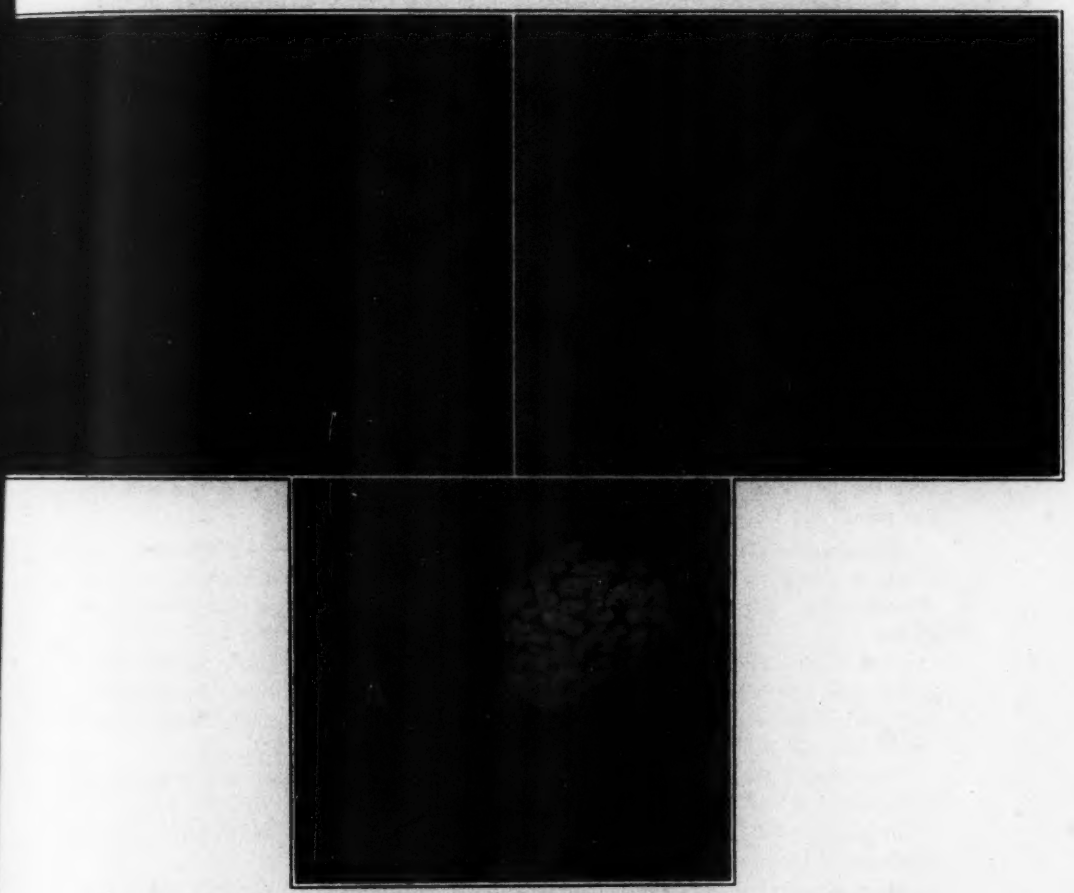

Fig. 7 (case 1).—*A*, a diagrammatic sketch of the lesions before treatment: The larger one extends from the temporal margin of the disk to well beyond the macular region. There is a smaller lesion below the disk. *B*, a diagrammatic sketch of the lesion after about half the treatments: The larger lesion is reduced considerably in size. The smaller lesion is hardly visible. *C*, a drawing of the larger lesion at the completion of the treatments: There is an elevated chalky white mass with undulating surface and irregular borders. At the upper and lower borders there is a pigmentary disturbance.

up of thick white strands, and the margins had become irregular as though fluid or some uneven substance occupied this portion. The smaller lesion below the disk had definitely changed to a small white plaquelike area.

In June 1933 (about two months later) the parents stated that they had noticed continued improvement in the vision and in the general health. The ophthalmoscope showed that the tumor had been reduced to a white glistening plaquelike mass, sharply defined, with apparent organization changes in the form of irregularly crossed portions. The entire mass was a little more definitely located above the macula, although reaching to and involving it. The smaller mass below the disk had almost disappeared (fig. 7 *B*).

The examinations were continued (always under general anesthesia) at intervals of from one to two months. The tumor gradually decreased in size, and the surface became more irregular in contour. As the lesion became smaller and less vascular, it appeared whiter. At the last examination, in December 1935, the mass was reduced to a slightly elevated glistening white area with irregular borders, surrounded by a zone of pigmentary disturbance. The last notation of a change in the appearance of the growth was made in February 1934, one year after the beginning of treatment. Since no further change was noted, the treatment was discontinued three months later, in May 1934 (fig. 7 *C*). At the present time (December 1935), almost three years since the beginning of treatment, the child has gained in weight (now weighing 33½ pounds [15.25 Kg.]). She has a good memory, is very active and plays normally with other children. The head is slightly tilted to the left, especially when she is intently observing objects. Although a trifle undersized, she has good color. The fundus of the eye is quiet, with only the organized lesion present. The visual acuity is 10/25 (pictures).

Case 2.—L. C., aged 5 years, was referred by Dr. John M. Wheeler in September 1933. In July 1933 the boy had sudden severe pain in the left eye and over the left side of his head. The mother noted that the eye was red and that the pupil was larger than that of the fellow eye.

Examination.—Right Eye: There was complete detachment of the retina, with a tumor filling the nasal half of the vitreous cavity. The intra-ocular pressure was elevated. A roentgenogram of this eye showed the presence of calcium in the globe.

Left Eye: There was a round grayish to yellowish-white mass in the retina at the equator between 3 and 5 o'clock (fig. 8 *A*). The mass measured 7 to 8 diopters high and about 4 disk diameters across. The fundus elsewhere appeared normal. There was no elevation of intra-ocular tension.

The clinical diagnosis was retinal glioma in each eye and secondary glaucoma in the left.

In August 1933, the left eye was enucleated by Dr. John M. Wheeler at the Institute of Ophthalmology of the Presbyterian Hospital.

Pathologic Report on the Left Eye.—The cornea is ectatic and the sclera seems thinned. The iris shows considerable atrophy, and there is partial replacement of its stroma by connective tissue. An extensive peripheral anterior synechia obliterates the angle of the anterior chamber and deepens the posterior chamber. A small degree of ectropion of the uvea is present. The ciliary body is atrophic. Extending forward from the disk with the latter as a broad apex is a wedge-shaped mass of tumor, which replaces the atrophic remains of a completely detached retina. The main body of the tumor consists of large nodules, cords and cylinders of tissue surrounding axial blood vessels. There are large areas of degeneration and necrosis between the cords of living tumor cells, with a great deal of calcium

deposited and a few hemorrhages. The tumor cells are small, often cylindric or spindle-shaped, with large oval or round nuclei. Some mitotic figures are noted. Scattered through the tumor masses are groups of golden-brown pigment granules. Masses of tumor cells are seen in the vitreous and in the large amount of sub-

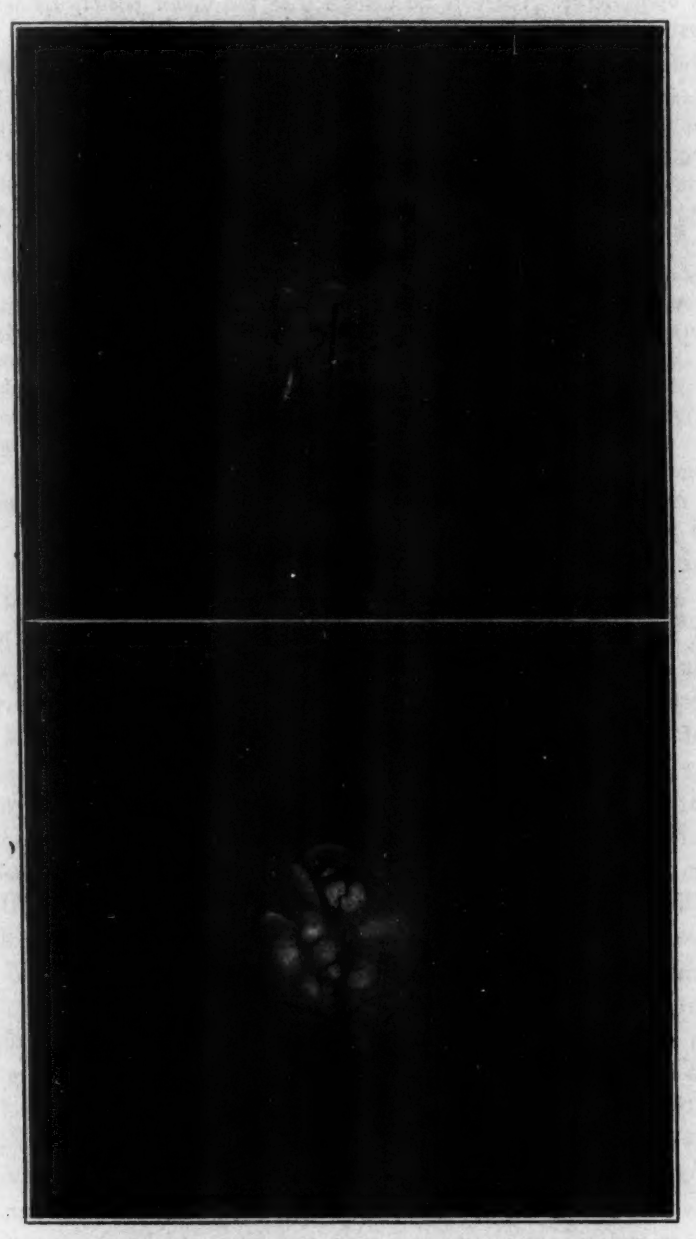

Fig. 8 (case 2).—*A*, the ophthalmoscopic appearance of the lesion before treatment: (*a*) well demarcated white foci which probably represent areas of calcium. *B*, the ophthalmoscopic appearance at the completion of treatment: (*a*) a slightly elevated chalky to pearly white mass; (*b*) pigmentary changes.

retinal fluid. Adjacent to the choroid are many nodules of tumor cells, often with necrotic centers. In several areas, the tumor has penetrated the lamina vitrea, forming flattened nodules in the inner choroid. The optic disk is cupped, and this is filled with tumor tissue which extends in strands through the lamina cribrosa into the optic nerve. There is no extension of the tumor posteriorly beyond the site where the nerve was severed at the operation.

Pathologic Diagnosis.—The diagnosis was retinal glioma of the left eye.

Treatment.—In September 1933, the patient was referred to the Memorial Hospital for irradiation of the right eye. Between Sept. 29, 1933 and April 15, 1935, the patient received seventy-three roentgen treatments, the doses varying in size from 300 to 400 r each, at the rate of two to three per week. The spacing of the treatments, the dose to each portal and the total period of the treatment are shown in figure 3.

Clinical Course.—Over the period of the first seven months there was steady regression of the lesion to what we thought was the final arrested stage. Treatment was therefore stopped and the lesion observed at regular intervals for ten months, during which time we noted no change. At the eleventh month, we thought there might be some increase in the vascularity and the circumference at one site of the lesion. As a precautionary measure we resumed treatment for two months. It has now been eight months since the last treatment, and no change has occurred in what we think is the arrested state of the tumor (fig. 8 *B*). The boy has vision of 20/20 and attends school, where he does satisfactory work with no apparent handicap.

CONCLUSIONS

As we have mentioned, we planned the radiation treatment in our present series of cases with the conviction that retinal glioma is radioresistant and not capable of control by small or even moderate doses in the average case. Since the principle of giving a few small or massive doses of radiation had not met with even reasonable success in the past we felt that a technic employing a highly fractionated large total dose would be worthy of trial. In order to spare the eye from the undesirable and even serious effects of a large dose of radiation, we have used small circular portals, accurately directed so as to confine the beam of roentgen radiation as much as possible to the region of the growth itself. We have applied the radiation as frequently and in as large doses as was compatible with the maintenance of the integrity of the local normal structures and with the health and comfort of the child. Up to this time, in a series of six consecutive cases, we have had no failures. Two patients are approaching the three year period of control of the disease with satisfactory vision in the treated eye.

This preliminary report of a therapeutic method is not intended as final proof of its merit in the permanent control of retinal glioma, which must await the time when several cases have passed the five year period. The exact technic which we use may not prove to be the most perfect in all its details, which may be modified and we trust improved in the future.

DISCUSSION

DR. BEN WITT KEY: Since it is well known that the course of this disease (retinoblastoma) from its onset to its fatal termination extends over several years, we cannot be content to claim that we have in this case a final cure of the disease; but I feel sure that I should have failed to do my duty if this case had not been reported now, when at almost 4 years of age the child appears to have completely recovered, for two years past having had no treatment whatever and having been without any ocular or general recurrence.

It is worthy of note that this child received treatments for sixteen months, the last in June 1934, and that forty-eight treatments were administered—10,000 r to the temporal region and 2,400 r to the nasal region. This form of treatment over a period of time, with not more than eight applications a month and then a delay of a month or two, seems just as effective if not more so than treatment applied every month from eight to ten times each month. Some of these gliomas have not responded as promptly as those to which the treatments have been applied over a longer period of time. Is it that the dosage is too intensely administered or that repeated applications are irritating to the lesion?

The effect of the fractional or divided dose principle of roentgen irradiation as it was administered in these cases was to produce the reaction of the skin over the temporal region that may be noted to be the characteristic radiation burn; there is also atrophy of the temporal muscle, as evidenced by the depression in this region. In the roentgenographic plates the temporal portion of the bony orbit is thinned and almost invisible. Does this mean that there is atrophy or absorption or failure of development of the temporal bony rim of the left orbit as the result of irradiation? But the orbit of this eye is larger than that of the fellow eye. This, however, may be due to the removal of the right eye at the age of 8 weeks.

The brow, the lids and the cilia of this child are undisturbed by the treatment, no deformity whatever resulting. The conjunctiva remains normal; the cornea and iris likewise are unaffected. There is no redness, no burn or other defect. It is important to note that the lens is clear and transparent, having apparently escaped opacification from the radiation applied so skilfully by Dr. Martin.

The ophthalmoscope reveals only absorption and organization changes in the glioma, resulting from destruction of the tumor cells by the radiation treatment. No hemorrhage occurred, no blanching of the retina, even where the tumor cells were known to have been present. This is especially noticeable in the small area of involvement below the disk in my case, shown before the application of roentgen radiation. This small area now has almost disappeared, and only a glimpse of pigmentation can be made out.

It is unnecessary to review here the pathology of the cell death, absorption and organization which evidently take place in a glioma when roentgen radiation is successfully applied. The depressed or thin margins of the tumor as demonstrated by the fundus drawing which I made in April 1933 (about two months after radiation was applied)

show that liquefaction had taken place—cellular death, the breaking down of lymphatic or newly formed blood vessels and partial absorption of this tissue having taken place. This, together with the final result of organization, fibrosis and probably calcification of the glioma, may be observed by roentgen and by ophthalmoscopic examination.

As interesting and as important as this case may seem to be, the fractional or divided dose principle of radiation therapy in the hands of Dr. Hayes E. Martin seems even more interesting and more important. To say that I congratulate Dr. Martin is to put it mildly. No word of praise can be found in the dictionary to state fully what his efforts, study and work deserve. It is my opinion that the result which he has secured in this case is truly epoch-making.

Dr. John M. Wheeler: My part in this work has been simply the furnishing of some of the patients, and Dr. Reese has reported the results. Like Dr. Key, I feel more excited about this than Dr. Martin appears to. I think that the results are wonderful, and I do not feel in as conservative a mood toward the matter as do Dr. Martin and Dr. Reese. Formerly, confronted with bilateral glioma, we were in a hopeless state of mind. We did not know what to advise. With one eye well in the lead in the gliomatous process, and that is the usual situation, we now know that the chances may be good for the eye with the lesser involvement, and we can really be a bit optimistic, I think.

Dr. Martin will probably forgive me if I say something about his attitude toward the work of other men who have used radiation for retinal glioma. I am sorry that he discredited the work of other men, particularly in reference to the patient whom Dr. Schoenberg has shown here, a girl who nineteen years after treatment with radiation is well. She has had some unfortunate results from the use of radium but she is a cured patient in whom a glioma of the retina had been demonstrated. For Dr. Martin to say in regard to patients treated by other men that either there was spontaneous recovery or the gliomas were unusually sensitive to radiation is, I think, rather unfortunate. To be sure, Dr. Schoenberg's patient has a disturbance of pigment which is characteristic of the action of radiation on the skin. She lost eyelashes, she lost an eyebrow, she had a cataract, and those things are unfortunate, but the glioma is gone.

With Dr. Martin's method, the dosage can be accurately controlled and the rays can be accurately directed, and the results are wonderfully good. I think it would be unfortunate if somebody should say in regard to these results that either there was a spontaneous recovery or the gliomas were especially sensitive to radiation.

I should like to ask two questions: First, do Dr. Ewing and Dr. Reese think that "glioma" is the best term to use in designating the type of tumor which has been discussed tonight, or is "retinoblastoma" or some other term better? Second, when enucleation has been performed for a glioma of the retina and it has been demonstrated that there are tumor cells in the excised nerve and that there probably are tumor cells in the remains of the nerve in the orbit, would it show better judgment for the surgeon to make an entrance to the orbit and remove some of the remaining nerve, or would it be best to rely on radiation for the treatment of any remaining cells in the optic nerve?

I should say one is now in this position: If in a case of glioma of the retina there is a considerable portion of retina which is uninvolved the method of choice is irradiation of the growth by Dr. Martin's technic. In the case of a relatively small glioma which is unilateral I should say that roentgen irradiation might be preferable to enucleation.

DR. JAMES EWING: It seems to me obvious that the authors of this communication have made a contribution of first class importance both in ophthalmology and in general roentgen therapy. It appears that the old problem of the successful treatment of glioma of the retina with preservation of sight has reached at least a partial, if not complete, solution. The attempt to control this malignant neoplasm has continued many years, has called for much ingenuity, leading to many trials and errors, with occasional successes and more failures, until adoption of the present use of small doses through small portals over a protracted period. I well recall the early failures and the disappointment when the radiosensitivity indicated by the structure was not realized and the tumors proved generally radioresistant. Then came the failures and disasters from the use of the massive doses which seemed to be demanded to kill cancer cells. Dr. Martin deserves great credit for employing skilfully the Coutard method of administering the divided doses, but, in addition to that, he has improved on the method in an essential particular by employing multiple small portals. By the ordinary Coutard method, even extended over months, one could never give 15,000 r without damaging the tissues of the orbit; yet after these enormous doses have been delivered through small portals the eye and orbital tissues are in an excellent state of nutrition. This is a great advance in roentgen therapy, which is applicable to many tumors.

The treatment of glioma of the retina has passed through many stages of experiment. I would point out that there are other major forms of cancer, more important than glioma of the retina, the radiation treatment of which is in the experimental stage, and that the attitude of those who are not engaged in working out such problems should be sympathetic and encouraging, since at any time success may be attained in new fields.

Dr. Martin raises a doubt about the genuineness of the few cures by irradiation previously reported; he argues that they were probably spontaneous regressions. He calculates that the doses delivered were far too small to have affected these tumors seriously. Dr. Wheeler regrets that this question was raised, since it may be unfair to those who treated the patients. I share to some extent Dr. Wheeler's feeling. The sensitivity of retinal glioma probably varies, and it seems possible that in rare cases small doses give a paradoxical cure. In ordinary glioma of the retina the radioresistance depends on the blood supply, and the destruction of the tumor must result from closure of the blood vessels, infarction, atrophy and calcification, and not by the direct killing of tumor cells. In patients with a narrowly balanced circulation, it seems possible that the circulation might be upset by rather small doses. However, Dr. Martin is speaking as a radiotherapeutist who dreads above all things self-deception, reliance on partial regressions of tumors and the use of methods which work only occasionally, and from this practical point of view I think he is wise to warn against reliance on the methods employed in the cases referred to.

Since a reliable method of treating glioma of the retina now seems available, ophthalmologists face a difficult and urgent task in securing early recognition of the disease. Dr. Reese states that in the great majority of cases the patient does not reach the doctor until the eyeball is filled with tumor tissue. Yet an alert parent can recognize the condition in its early stages. One mother reported that she saw a silvery reflection in the eye of her 3 month old infant, which was probably caused by the early deposit of calcium in the tumor. Is it not possible by education of parents, physicians, ophthalmologists, nurses, children's attendants, teachers and all those brought in contact with infants to recognize this silvery reflection or other symptoms so that the condition may be diagnosed early enough to adopt Dr. Wheeler's suggestion that irradiation of the growth is now the treatment of choice?

Finally, I wish to express my preference for the old term "glioma of the retina" over "retinoblastoma." I see no excuse for the introduction of the term "blastoma" for any tumor unless it refers to one of strictly embryonal tissue. "Blastoma" signifies tumor of mother cells, but the glioma of the retina does not arise from mother cells but from adult cells of the nuclear layers, as long ago determined by the early observers in the nineties.

DR. MARK J. SCHOENBERG: Some nineteen years ago a baby with bilateral glioma of the retina, about 6 months old, was brought to my office. The parents had noticed a whitish reflex in the pupillary area of the left eye. Examination revealed a glioma of the retina filling the entire vitreous cavity of that eye. After prolonged search I found two masses in the right eye, one in the lower nasal sector of the retina and the other in the periphery above. It took about six months before I could persuade the mother to have the right eye enucleated. After the operation, I referred the patient to the general division of the Memorial Hospital, and the child had three treatments with radium and apparently got well, or I could not have presented her here tonight, after a period of nineteen years. The vision in that right eye is 20/30. The details of the case may be read in the ARCHIVES OF OPHTHALMOLOGY (**56**: 221 [May] 1927). One of the gentlemen here, a very experienced ophthalmologist, questioned whether the patient is cured after nineteen years. He thinks there is still a possibility that there is a little nest of cells in the mass which was visible in the lower nasal quadrant of the fundus. This white mass, covered by blood vessels, has remained stationary during all these years. Perhaps he is right. I have no way to disprove that, but I think that Dr. Ewing, the distinguished pathologist who happens to be here tonight, would say that a patient with a glioma which has remained stationary for nineteen years can be considered cured.

This leads me to the question whether Dr. Reese's patients are cured. He has had two of them under observation for from two to three years, and, while I do not like to be a pessimist, I think it would be advisable to show the patients again a few years later. The gliomas in the two children whom I have examined tonight look a little different from that in my own patient. I mention this because it has clinical importance. The glioma in my patient from the very first, even before it was treated, had a zone of choroidal atrophy and pigmentation about one-eighth disk diameter broad all around it. The masses that I have

seen in the two children have no such zones of chorioretinal reaction. There is no doubt that there are various types of glioma of the retina; some of them respond very easily to radiation; others are entirely resistant to it, and some of them are between the two. The information furnished by pathologists is of great value, but the clinical study of types of glioma is also of great importance. The two cases presented this evening do not represent all the clinical types of glioma of the retina.

Dr. Wheeler has mentioned the "unfortunate" results with the old treatment by means of "massive" doses. True, a "massive" dose may cause loss of hair, a burn of the skin and cataract. Cataract is the most serious complication. I had to extract a cataract from the eye of my patient, but the result is very good. I wish to ask Dr. Reese whether he has studied the eyes of these children with the slit lamp. I know this is very difficult, because children do not behave and one cannot make a careful study with the slit lamp, but without an examination by means of the slit lamp one cannot know whether a roentgen ray cataract is or is not really beginning to develop. One great disadvantage of the fractional method is the length of the total period of treatment. This is six months, a year or even more. The patient has to be brought to the clinic several times a week—not a simple matter for poor people. During such long periods, one is likely to lose half of one's patients—and that would be a tragedy. With the old way of treating (my patient had only three applications) the number of calls is limited.

There is an important point which should be brought out for the benefit of the younger men in this audience, and that is that it is extremely important to examine both eyes with the pupils dilated ad maximum and the child under general anesthesia. Another important point is the fact that the general practitioner does not know that a gliomatous eye may cross. To him a squint is a squint, and almost invariably he advises the parents to wait a few years before taking the child to an ophthalmologist. He does not know that a squinting eye may be the seat of a very serious lesion.

I have frequently noticed on the surface of a retinal glioma whitish, glistening areas which consist, as Dr. Reese has shown tonight, of calcium.

I should like to compliment Drs. Reese and Martin on their interesting work.

Dr. Algernon B. Reese: Dr. Key stated that the roentgenograms of the untreated eye in his patient did not show calcium. I believe that if these were taken in the usual manner they could not be expected to show calcium. Dr. Raymond Pfeiffer has given his attention to demonstrating the presence of calcium in retinoblastomas, and he finds that a special technic is required. I feel confident that the bulk of the lesion that now exists in Dr. Key's patient is calcium.

Dr. Wheeler has asked whether surgical operation or irradiation is indicated when glioma tissue exists in that portion of the optic nerve remaining in the orbit after enucleation. I should like to have Dr. Martin answer part of this question by stating whether or not he thinks irradiation would be effective. If so, I think this would be the treatment of choice.

Dr. Wheeler has inquired about our use of the term "retinal glioma." We have employed this term because Dr. Ewing favors it. He has given his reasons for preferring it.

We agree entirely with Dr. Schoenberg's statement that it is too early to regard these results as final cures. We hope to give a later report on all the cases. We did not examine the lenses with the slit lamp. We agree with Dr. Schoenberg that there may be incipient changes which we are unable to detect with the ophthalmoscope.

Dr. Hayes E. Martin: I regret that Dr. Wheeler has gained the impression that we intended to discredit the previously reported cures. Certainly that was not our intention. The cures are no doubt genuine in that the tumors regressed. Our purpose was to bring out the fact that except in one case in which the cure had been observed for five years and one in which the cure had been observed for three years the doses of radiation received were so small that they could cause complete regression only in exceptionally radiosensitive tumors. It will be generally agreed that retinal glioma is comparatively radioresistant. Is it not significant that the gliomas treated by us regressed only after the application of from thirty to fifty times the doses delivered to all except two of the gliomas reported cured by other technics?

The total number of gliomas reported to have shown spontaneous regression is several times that of the gliomas reported cured by irradiation; therefore, we feel that the possibility of spontaneous healing of glioma must be considered in connection with all cures by radiation, including our preliminary results. Dr. Wheeler has said that it would be unfortunate if some one were to say that some of our results were due to spontaneous regression. I do not feel that such a statement would be particularly unfortunate. The truth will come out when we report our percentage of five year cures in a series of consecutive cases, as well as in the final results of others who may employ our technic.

Dr. Wheeler has asked whether we advise irradiation or a surgical operation as the method of choice for postoperative treatment of a histologically demonstrated residual glioma in the optic nerve. We recently treated a patient, not included in this series, who was referred by Dr. John Bailey for prophylactic irradiation to the orbit after enucleation of the eye for a unilateral glioma. We gave this child a small dose of prophylactic radiation—a practice which is probably not very logical, although it has the sanction of long and general usage. During a six week interval of observation the mother noted the recurrence of a mass in the orbit from which the eye had been enucleated. The patient was sent back to us, and examination showed a recurrent mass at least 1 cm. in diameter, apparently growing from the nerve. Since we had no eye to worry about, we gave this child large daily doses with the small cylindric portal, previously described, and at the end of six weeks we implanted radon seeds in the residual tumor, which was still definitely palpable. The seeds were implanted about a month ago, and the last time we saw the child, a week or so ago, the mass had entirely disappeared to palpation. This patient is the only one in whom we have had the opportunity to treat residual disease in the nerve. It seems to me that in such a case as Dr. Wheeler mentions, the end

of the nerve might be surgically exposed and radon seeds implanted in it as soon as the presence of glioma has been verified in the segment attached to the enucleated eye.

We are gratified to learn that Drs. Wheeler, Key and Ewing feel that the results we have obtained justify the use of radiation alone in the treatment of unilateral glioma. From the practical standpoint, however, one must consider that the disease is usually not discovered until one eye is so extensively involved that no return of retinal function can be expected, even if the growth is permanently controlled by irradiation. In such cases, the advantages of the use of irradiation over surgical intervention are mainly cosmetic. We should welcome the opportunity to treat a small unilateral glioma by irradiation alone.

Dr. Ewing has emphasized the importance of early diagnosis and of the education of parents, physicians, ophthalmologists, nurses and children's attendants in the recognition of the early symptoms. Unfortunately, the age of the patients precludes the discovery of subjective symptoms. Objective symptoms usually indicate an advanced stage of the disease.

We wish to thank Dr. Key and Dr. Wheeler for sending us their patients to treat. We realize that retinal glioma is rare, and we are grateful for the unusual opportunities afforded us in this investigation.

BIOCHEMISTRY OF THE LENS

IX. INFLUENCE OF VITAMIN C AND SULFHYDRYLS ON THE PRODUCTION OF GALACTOSE CATARACT

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CHICAGO

The ability to produce cataract in the albino rat at will by a nutritional method offers a means for the study of factors influencing its production. Such a method was made available by the report of Mitchell and Dodge [1] that cataracts developed in rats fed on a lactose diet. This report was confirmed and extended to show that galactose produced cataracts much more rapidly than lactose (Mitchell,[2] Dodge [3] and Yudkin and Arnold [4]).

The galactose cataract has been explained by Mitchell as the result of injury to the epithelium of the lens by this sugar. Her assertion is based on the observation of Kirby and his collaborators [5] that a low concentration of a solution of galactose (as compared to that of a solution of dextrose) is toxic to tissue cultures of lenticular epithelium. She believes that as a result of the injury to the lenticular epithelium there is an increased permeability of the membrane of the lens to the various inorganic ions. Thus she found the calcium content of such cataractous lenses to be three or four times that of lenses of control rats fed on corn starch. Yudkin and Arnold offered another explanation, which is as follows: Galactose causes a disturbance of the calcium metabolism in the body, or its presence in the intestines brings about an absorption of calcium so as to cause a lack of this substance for the combination with and detoxification of foreign substances which when absorbed exert a toxic effect on lenticular tissue.

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1. Mitchell, H. S., and Dodge, W. M.: J. Nutrition **9**:37, 1935.

2. Mitchell, H. S.: Proc. Soc. Exper. Biol. & Med. **32**:971, 1935.

3. Dodge, W. M., Jr.: Histopathologic Characteristics of Nutritional Cataract in the White Rat, Arch. Ophth. **14**:922 (Dec.) 1935.

4. Yudkin, A. M., and Arnold, C. H.: Cataracts Produced in Albino Rats on a Ration Containing a High Proportion of Lactose or Galactose, Arch. Ophth. **14**:960 (Dec.) 1935.

5. Kirby, D. B., and Wiener, R. von E.: Tr. Am. Acad. Ophth. **37**:142, 1932. Kirby, D. B.; Estey, K., and Wiener, R. von E.: ibid. **37**:196, 1932.

A more likely explanation is that galactose is toxic to lenticular tissue because it produces a disturbance of the internal oxidative mechanism. As will be shown in this report, the cysteine (and glutathione) content of the crystalline lens diminishes in rats fed a high galactose diet. Further proof of this is that in rats on a galactose diet plus cysteine cataracts do not develop as rapidly as in control rats on a galactose diet without cysteine. Since it is well established that the sulfhydryls (cysteine and glutathione) and vitamin C are essential for the internal oxidative mechanism of the lens, it can be readily appreciated that any substance causing a loss of one or both of these essential substances may be toxic to the lens and cause its death. A somewhat similar circumstance pertains to naphthalene cataract in rabbits. Bourne and Young [6] have shown that in this case cysteine is conjugated with naphthalene and is excreted as a derivative of mercapturic acid. The lens becomes depleted of this essential factor, and cataract forms. Bourne [7] showed that in rabbits on a diet of cabbage and oats cataract did not develop as readily as in control rabbits receiving carrots and bran. Her explanation is that the former diet is richer in calcium and that this in some way prevents the cataract. Judging from the experiments reported here on galactose, the mechanism is probably as follows: Cabbage is much richer in vitamin C than carrots. Therefore, as the cysteine in the lens is lost vitamin C replaces it and helps to perform a greater part of the oxidation and reduction function than it ordinarily does. In this way the lens is kept viable. Further work along this line is contemplated.

Working on the hypothesis that galactose interferes with the internal oxidative mechanism of the lens, I wished to ascertain whether an excess of vitamin C or cysteine in the diet would delay or prevent cataract in rats fed on galactose and, second, whether a diminution of these substances occurs in the lens before the onset of lenticular opacities.

EXPERIMENTS

EXPERIMENT 1.—The purpose of this experiment was to produce cataracts in albino rats by feeding a diet high in galactose. Two litters of seven rats each, aged 6 weeks and weighing from 55 to 65 Gm., were used. The rats in litter 1 received a diet consisting of 70 per cent galactose, 15 per cent casein, 9 per cent hydrogenated oil (crisco), 2 per cent cod liver oil, 4 per cent salt mixture and vitamin B (yeast powder, 0.5 Gm. daily). The rats in litter 2 were fed on a similar diet except that the galactose was replaced by corn starch.

Results.—Within seven days the rats in litter 1 showed opacities of the lens which became confluent and finally turned whitish gray at the end of from seventeen to nineteen days. The rats in litter 2 showed no change in the lens detectable by means of the ophthalmoscope.

6. Bourne, M. C., and Young, L.: Biochem. J. **28**:803, 1934.
7. Bourne, M. C.: Brit. J. Ophth. **17**:210, 1933.

Interpretation.—This experiment confirms the reports of Mitchell, Dodge and Yudkin and Arnold that a diet rich in galactose produces cataract in the albino rat.

EXPERIMENT 2.—The effect of injections of vitamin C on rats receiving galactose was tested. Four rats aged 6 weeks and weighing from 55 to 65 Gm. were fed a diet 50 per cent of which was galactose. Two rats received 50 mg. of vitamin C in crystalline form intraperitoneally daily. Two rats were used as controls.

Results.—Within seven days all the rats showed peripheral lenticular opacities. At the end of twenty-three days in the two control rats mature whitish cataracts had developed. The rats receiving vitamin C did not show this condition (fig. 1). At the end of twenty-five days bilateral whitish cataracts had developed in one rat receiving vitamin C. The second rat receiving vitamin C did not show whitish opacities until the end of thirty days.

Fig. 1.—*A*, appearance of lens of a rat receiving galactose (control), after twenty-three days. *B*, appearance of lens of a rat receiving galactose and vitamin C, after twenty-three days. Note the complete opacity of the lens in *A*, which is not seen in *B*.

Interpretation.—Although it is well known that rats under ordinary conditions produce sufficient amounts of vitamin C to be independent of exogenous sources, an excessive amount is utilized in some way to delay the onset of cataract in rats receiving galactose.

EXPERIMENT 3.—The purpose of this experiment was to determine whether yeast, which is rich in glutathione, will delay the onset of cataract. Twelve rats, aged 7 weeks, weighing from 60 to 75 Gm., were used. Group 1 consisted of four rats receiving a diet of 70 per cent galactose plus 10 per cent corn starch. Group 2, received the same diet as group 1 but in addition received 50 mg. of vitamin C intraperitoneally daily. Group 3 consisted of four rats receiving a diet of 70 per cent galactose plus 10 per cent yeast.

Results.—Within seven days the rats in group 1 showed peripheral opacities of the lens. The rats in groups 2 and 3 showed no lenticular change detectable with the ophthalmoscope (fig. 2 *A*).

On the ninth day the lenses of the rats in group 1 gave a dark reflex with the ophthalmoscope, except in the pupillary area. (The peripheral opacities had become confluent and had extended centrally.) The rats in groups 2 and 3 were beginning to show peripheral opacities of the lens, which were more marked in the former (fig. 2 *B*).

On the tenth day the eyes of the rats in group 1 were unchanged. In the rats in group 2 the opacities of the lens were more advanced than on the preceding day, whereas the rats in group 3 showed the slightest change (fig. 2 *C*).

On the twelfth day the lenses of all the rats in groups 1 and 2 showed a dark reflex with the ophthalmoscope. The lenses of the rats in group 3 showed only peripheral opacities (fig. 2 *D*).

On the fifteenth day the lenses of all the rats of group 1 (the control rats) showed whitish opacities visible with the naked eye. The lenses of the rats in group 2 showed a dark reflex with the ophthalmoscope. The rats in group 3 showed only peripheral opacities of the lens (fig. 3).

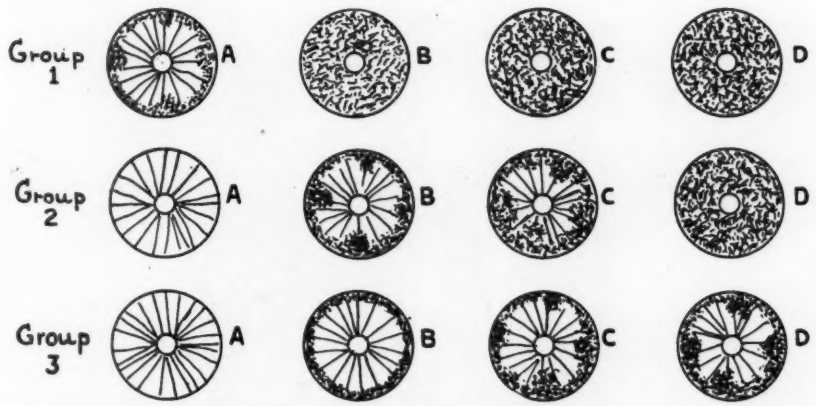

Fig. 2.—Comparison of the ophthalmoscopic appearance of the lenses of rats receiving galactose (group 1), those of rats receiving galactose and vitamin C (group 2) and those of rats receiving galactose and yeast (group 3). Note that the lenses in group 1 are the first to become opaque; those in group 2 become opaque later and those in group 3 last.

On the seventeenth day the lenses of two of the rats fed vitamin C showed whitish opacities visible with the naked eye. The lenses of the others in this group showed a dark reflex with the ophthalmoscope. The lenses of the rats in group 3 showed no further change.

On the eighteenth day all the rats in group 2 (those given vitamin C) had whitish opacities of the lens. The lenses of the rats in group 3 (given yeast) showed a dark reflex with the ophthalmoscope.

On the twenty-first day the lenses of the rats in group 3 showed whitish opacities.

Interpretation.—The onset of cataract in rats on a galactose diet seems to be somewhat delayed by the intraperitoneal injection of large doses of vitamin C. This effect is even more definite with the adminis-

tration of yeast. Experiment 4 was undertaken to determine whether the effect of the yeast was due to its sulfhydryl content (cystine) or to some other factor.

EXPERIMENT 4.—The purpose of this experiment was to determine whether cystine will prevent or delay the onset of the galactose cataract. (The concentration of the galactose in the diet was reduced to 35 per cent because it was thought that a greater interval would elapse between the onset of cataract in the control rats and those receiving sulfhydryls in the form of cystine.)

One litter consisting of six rats, aged 6 weeks and weighing from 55 to 65 Gm., was placed on a 35 per cent galactose diet. Three of the rats received 0.3 per cent cystine in their diet.

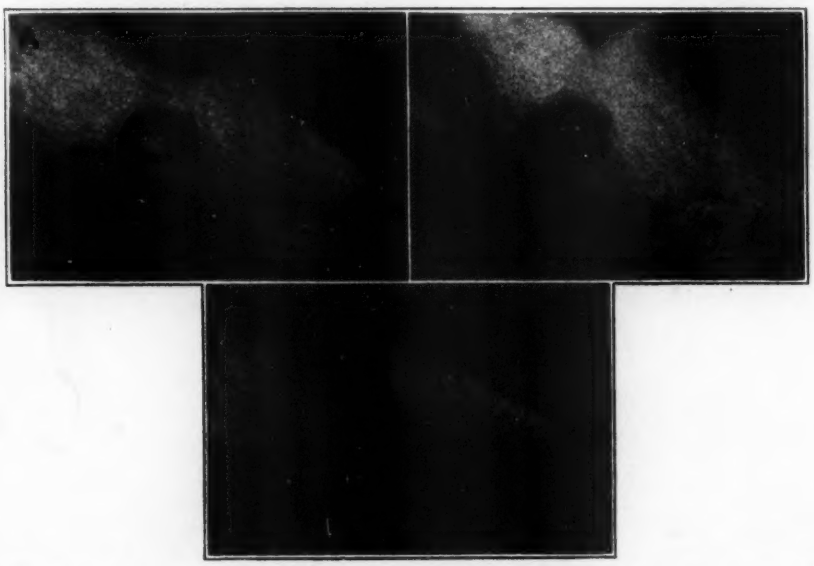

Fig. 3.—*A*, appearance of lens of a rat receiving galactose (group 1), after fifteen days. *B*, appearance of lens of a rat receiving galactose and vitamin C (group 2), after fifteen days. *C*, appearance of lens of a rat receiving galactose and yeast (group 3), after fifteen days. The lens in *A* is completely opaque; that in *B* shows beginning opacity, and that in *C* is clear.

Results.—On the seventh day the lenses of all the control rats (not given cystine) showed peripheral opacities, while only one rat receiving cystine showed lenticular opacities.

On the ninth day the lenses of the control rats showed confluence of the peripheral opacities and extension centrally. Only one rat receiving cystine showed peripheral opacities of the lens; the lenses of the others were normal (fig. 4 *A*).

On the tenth day the lenses of the control rats showed a dark reflex with the ophthalmoscope. Peripheral opacities of the lens appeared in the lenses of all the rats given cystine (fig. 4 *B*).

On the thirteenth day the appearance of the lenses of the control rats showed no further changes. The peripheral opacities in the lenses of the rats given cystine had extended somewhat centrally (fig. 4 *C*).

On the seventeenth day three lenses of the rats given cystine showed a dark reflex. In the other three eyes the opacities of the lens were incomplete.

On the eighteenth day one of the lenses of one control rat showed a grayish white opacity. The lenses of the remaining control rats still showed a dark reflex. The lenses of all the rats given cystine showed a dark reflex when viewed through an ophthalmoscope.

On the twentieth day both lenses of one of the control rats showed a grayish white opacity. There were no further significant changes in the eyes of the other rats.

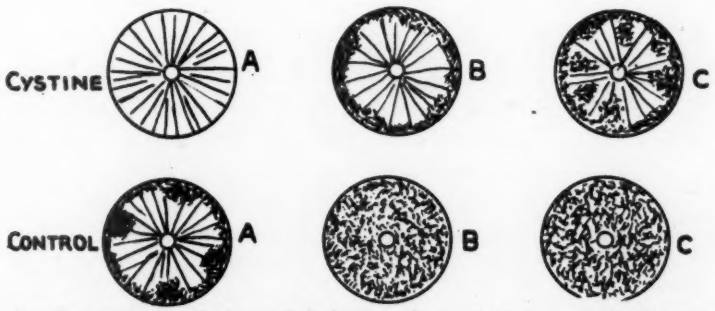

Fig. 4.—Comparison of the ophthalmoscopic appearance of the lenses of rats receiving galactose and cystine and those of rats receiving galactose alone. Note that the lenses of the rats receiving cystine remained clear much longer than those of the controls.

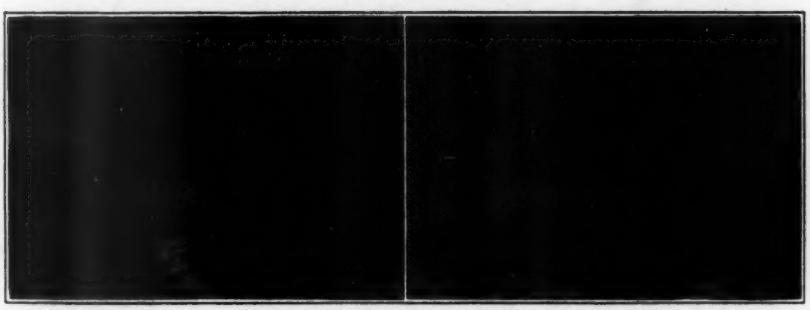

Fig. 5.—*A*, appearance of lens of a rat receiving galactose (control), after twenty-seven days. *B*, appearance of lens of a rat receiving galactose and cystine, after twenty-seven days. The lens in *A* is completely opaque; that in *B* is not.

On the twenty-fifth day both lenses of two of the control rats showed whitish opacities. There was no change in lenses of the group given cystine.

On the twenty-seventh day all the control rats (three) had bilateral whitish opacities of the lens. One rat in the group given cystine showed a whitish opacity in one eye (fig. 5).

On the thirty-sixth day both lenses of one rat in the group given cystine showed opacities; one lens of one rat showed a whitish opacity. The lenses of the third rat showed only a dark reflex with the ophthalmoscope.

On the thirty-ninth day both lenses of all three of the rats given cystine showed whitish opacities.

Interpretation.—The fourth experiment shows that a small excess of cystine added to a diet rich in galactose delays the time of onset of cataract in the rat as compared with the time required in control rats. This must mean that the sulfhydryls in the crystalline lens are lost or destroyed by the presence of galactose and that an excess of these substances in the diet will delay the death of the lens fibers either by replacing or by sparing those which are in the lens. Further proof of

TABLE 1.—*Results of Feeding Experiments*

Diet	Number of Rats	Number of Days Before Opacities of the Lens Appeared as Seen with the Ophthalmoscope	Number of Days Before Whitish Opacities of the Lens Were Plainly Visible to the Naked Eye*
70 % galactose	7	7	17-19
70 % corn starch	7	No change	No change
50 % galactose plus vitamin C daily (50 mg.)	2	7	25-30
50 % galactose (control)	2	7	23
70 % galactose plus 10 % corn starch	4	7	15-17
70 % galactose plus vitamin C	4	9	17-19
70 % galactose plus 10 % yeast	4	9	21-23
35 % galactose	3	7	18-27
35 % galactose plus 0.3 % cystine	3	7-10	27-39

* The first number in the last column represents the number of days required for the first cataract to appear; the second number represents the number of days required for the entire group to show cataracts.

TABLE 2.—*Amounts of Vitamin C and Glutathione in Lenses of Rats on a Normal Diet and Rats on a Galactose Diet*

	Number of Rats	Glutathione, Mg. per Gm.	Vitamin C, Mg. per Gm.
Normal diet	3	2.570	0.082
35 per cent galactose diet for 3 days*	3	2.090	
35 per cent galactose diet for 6 days*	6	0.714	0.083
Rats with immature galactose cataract	3	0.511	0.072

* Ophthalmoscopic examination disclosed no changes in the lens.

this point would be the finding of a diminution in the amount of sulfhydryls or vitamin C in the lens before the appearance of lenticular opacities. (It is well known that these substances are diminished in amount in the cataractous lens.) If it could be shown that they diminish in amount before the opacities in the lens appear, this, coupled with the fact that an excess of these substances in the diet delays the onset of opacities, would make it reasonably certain that the loss of these substances is responsible for the cataract formation. To prove this the following experiment was performed:

EXPERIMENT 5.—The purpose of this experiment was to determine the amount of vitamin C and glutathione in the lens of rats on a galactose diet.

Rats were placed on a 35 per cent galactose diet. At the end of three days and again at the end of six days the rats were chloroformed, and the lenses were removed. These were pooled, and the vitamin C and glutathione contents were determined. (The method used was described in a former report.[8])

As can be seen from table 2, the sulfhydryls (glutathione and cysteine) are diminished in quantity in the lenses of rats fed galactose, even before there is any visible change. There is little change in the content of vitamin C. This is as was to be expected, because vitamin C does not appear to be as effective in delaying the onset of the opacities as is glutathione or cystine. (The latter substances are known to be of importance in detoxification.) However, since vitamin C does delay the onset of the cataract to some degree, one is led to believe that the sulfhydryls and vitamin C are partially interchangeable in carrying out oxidation and reduction in the crystalline lens. Thus, as the sulfhydryl content diminishes, vitamin C, if available, will take over more and more of this function and will keep the lens more or less viable for some time. One may theorize that senile cataract in man may arise in a similar way, viz., as a result of a sudden or gradual loss of cysteine from the lens which is called on to detoxify various substances, along with insufficient replacement of these essential factors (vitamin C and cystine).

SUMMARY AND CONCLUSIONS

The reports of Mitchell and others that galactose in the diet of the albino rat produces cataract are confirmed here.

Galactose in some way causes a loss of the sulfhydryl content of the crystalline lens.

As a result of this the internal oxidative system of the lens reaches a stage where it is insufficient to support the life of the tissues. Death of the lens fibers occurs, with resulting opacification.

Cystine and, to a lesser extent, vitamin C delay the onset of this type of cataract.

8. Bellows, John: Biochemistry of the Lens: VII. Some Studies on Vitamin C and the Lens, Arch. Ophth. **16**:58 (July) 1936.

COMPLICATIONS OF THE FORCEPS INTRACAPSULAR OPERATION FOR CATARACT

BASED ON AN ANALYSIS OF FIVE HUNDRED SUCCESSIVE CASES

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As the intracapsular operation is being used by an increasing number of operators throughout the world, it seems of interest to examine the complications which have occurred in a series of 500 successive intracapsular operations to determine to what degree these complications can be ascribed to the method of operating and to study their significance and the possibility of their prevention.

This series includes every intracapsular extraction which I performed up to the completion of the 500 on May 15, 1934. The cases have been reported on in series of 100, and these reports have been published in the ARCHIVES OF OPHTHALMOLOGY.

The complications will be considered as they occur at the time of operation (group 1) or during the healing and later stage (group 2). The only complication in group 1 to be considered is prolapse of vitreous; the complications in group 2 are iridocyclitis, glaucoma and detachment of the retina.

GROUP 1

Of the 500 cases, vitreous was lost in 42; this is definitely a greater number than occurs with the extracapsular operation. The incidence of the loss according to the cases in hundreds is as follows: first hundred, 16; second hundred, 9; third hundred, 7; fourth hundred, 5; fifth hundred, 5.

Thus there was a definite improvement in the figures for loss of vitreous with each succeeding hundred cases. This is due to better anesthesia which was used in the operation for cataract and probably greater familiarity with the technic.

In considering prolapse of vitreous it is important to note in what stage of the operation the loss of vitreous occurred. Thus the loss occurred (1) directly after section in 5 cases, (2) during subluxation of the cataract in 12, (3) after delivery of the cataract in 12 and (4) at the end of the operation in 13.

Read at the meeting of the American Ophthalmological Society, Hot Springs, Va., June 2, 1936.

The loss of vitreous grouped according to the stage of the operation in each hundred extractions is shown in table 1.

This shows an improvement in the loss of vitreous in stages III and IV in the fourth and fifth hundred, i. e., in the stages following the delivery of the cataract and at the end of the operation.

Prolapse occurring directly after incision (stage I) is usually due to a dislocated lens, and vitreous is present in the anterior chamber. It is a complication which occurs in any type of extraction of cataract and so can be dismissed from this consideration. Vitreous was lost about equally in each of the other stages. Prolapse during subluxation (stage II) with this technic occurs when the capsule forceps dislocates the lens and ruptures the hyaloid membrane at the same time. The rupture of the hyaloid membrane may take place in any part of the circumference; this is noted by the appearance of a black gap between the pupillary margin and the cataract, with deepening of the anterior chamber. If this occurs the speculum should be replaced by retractors;

TABLE 1.—*Loss of Vitreous Grouped According to Stage of Operation*

Stage of Operation	First Hundred Extractions	Second Hundred Extractions	Third Hundred Extractions	Fourth Hundred Extractions	Fifth Hundred Extractions
I	1	..	1	1	2
II	5	..	1	4	2
III	5	5	2	..	..
IV	5	4	3	..	1

the capsule of the cataract is grasped again with the blunt forceps, and the dislocation is completed below and the lens extracted, often without additional loss, or, if this does not succeed, loop extraction must be done. The rupture of the hyaloid membrane may be due to the application of too much traction with the forceps or to an unexpected movement of the patient. In prolapse after delivery of the lens (stage III of the operation) the vitreous directly follows the lens as if it were adherent to it or because too much pressure was applied. In the final, or fourth, stage the loss of vitreous occurs in the process of replacing the columns of the iris or adjusting the conjunctival flap or on removing the speculum. The relatively large number of cases of loss of vitreous in the last stage of the operation is probably due to the fact that after extraction the vitreous body is deformed, extending forward, and is thereby readily injured by the spatula.

In some cases the capsule ruptures during the expression of the lens and has to be separately extracted; this may be followed by loss of vitreous. Presumably the rupture of the hyaloid membrane takes place at the same time that the capsule ruptures, or the hyaloid membrane may be adherent to the broken capsule.

The final vision in the cases of loss of vitreous was: 20/20 in 6 cases, 20/30 in 17, 20/40 in 5, 20/50 in 2, 20/60 in 2, 20/70 in 6, 5/200 in 2, perception of movements of the hand in 1 and perception of light in 1.

The poor visual result was due in part to maculae corneae in 2 cases (vision of 20/70), to central choroidal changes in 2 (vision of 5/200), to partial subchoroidal hemorrhage in 1 (vision of 5/200), to atrophy of the optic nerve in 1 (perception of movements of the hand) and to detachment in 1 (perception of light).

It is a mistake to minimize prolapse of vitreous. Loss of vitreous interferes with the healing of the wound and invites infection and inflammatory reaction. Fortunately, with the intracapsular operation the amount of vitreous lost is small, and the loss generally occurs after the delivery of the lens, so that no instrument need be introduced into the eye, and no trauma is done to the vitreous with resulting opacities and organizing bands. The fear that detachment of the retina may

TABLE 2.—*Cases of Iridocyclitis Grouped According to Severity of the Process*

Hundred Extractions	No. Cases	Mild	Updrawn Pupil	Severe
First	9	6	2	1
Second	6	6	..	..
Third	8	2	2	4 (1)
Fourth	4	1	..	3 (2)
Fifth	6	3	..	3 (2)
	33	18	4	11

follow is not justified; the small amount of vitreous lost cannot be a factor unless opacities of the vitreous or other inflammatory reactions follow and cause changes which lead to detachment. This phase will be taken up in the consideration of retinal detachment.

GROUP 2

Iridocyclitis.—The complication of iridocyclitis occurred in 33 cases. Iridocyclitis occurs with the intracapsular as well as with the extracapsular operation, but less frequently with the former, as the cortical remnants and capsular tags which are responsible for so many complications with the extracapsular operation are absent with the intracapsular procedure. In my series I noted that there were cases of mild iridocyclitis, of moderately severe iridocyclitis with synechia, an updrawn pupil and a thickened hyaloid membrane and finally a severe form, which includes a type which will be described in detail.

The cases may be grouped as shown in table 2.

It is well known that with the intracapsular operation there is little iritis; the pupil is easily dilatable; cortical remnants and inflammatory

thickening of the capsule are absent, and posterior synechia and opacity of the hyaloid membrane rarely develop.

I have included all the cases in which there was prolonged redness or symptoms of iritis or cyclitis. All the patients with the mild form recovered with good vision. Those with moderately severe involvement had posterior adhesions and a thickened hyaloid membrane; the resultant vision was fair, and discission or iridotomy was sometimes necessary. The severe forms include those which occurred in patients with poor general health, and the condition cannot be ascribed to this form of operation, though there were 5 cases in this group in which the method of operating may have been responsible (given in brackets in the tabulation).

This severe complication of iridocyclitis which has been observed in 5 cases is characterized by nonreformation of the anterior chamber and by the development or the persistence of an opacity in the deeper layers of the cornea accompanied by congestion and tearing. This is followed by vascularization of the cornea, iridocyclitis and, later, glaucoma.

This is the most serious complication which has been encountered in the cases in which intracapsular extraction was performed and is, I suspect, the reaction to traction on the ciliary body. This brings up the question of how much traction on the ciliary body the eye will stand. The important lesson to be learned is that if the cataract does not become dislocated readily on reasonable traction this procedure should be abandoned. This type of cyclitis must be traumatic; at the same time, certain eyes and patients with constitutional infirmities seem to be more disposed to it than others.

Glaucoma.—Glaucoma is an unusual complication with the intracapsular operation and is less frequent than in the cases in which the extracapsular operation has been performed. This is readily explained by the absence of anterior adhesions of the capsule to the incision, which is the usual cause for secondary glaucoma in aphakic eyes, though exceptionally glaucoma may follow an anterior adhesion of the hyaloid membrane.

Glaucoma was observed in 14 cases. In 4 cases it appeared at some time (several years) after the operation. In 6 cases it had been present before the cataract and was relieved by the operation for cataract. In 4 cases in which glaucoma was present before, the glaucomatous condition returned after the extraction of the cataract and had to be treated by drops or operation.

The intracapsular extraction of a cataract in cases of chronic glaucoma is usually characterized by easy subluxation of the cataract with the forceps. Glaucoma as a part of iridocyclitis is not considered under this heading.

Detachment of the Retina.—This occurred in 6 cases. The histories in brief are as follows:

In the first case (case 44 of the third hundred cases), that of a patient aged 63 with mature cataract, a good result was obtained with the intracapsular operation, though there were some opacities of the vitreous. One year later detachment of the retina developed. In the second case (case 78 of the third hundred cases), that of a patient aged 62 with hypermature cataract, extraction and healing were uneventful, but there were opacities of the vitreous. Vision was 20/20—. Eighteen months later detachment of the retina occurred. In the third case (case 31 of the fourth hundred cases) there was some iritis with disturbance of the vitreous; vision was 20/30. Two years later there was retinal detachment. In the fourth case (case 76 of the fourth hundred cases) the healing after operation was complicated by hyphemia and blood on the hyaloid membrane, which reduced the vision to 20/100. One year later detachment of the retina developed. In the fifth case (case 51 of the fifth hundred cases), that of a man 60 years of age with cataract in the posterior cortex, there was a slight loss of vitreous at operation. Vision at first was 20/30; there were opacities of the vitreous, and detachment of the retina occurred two months later. In the sixth case (case 100 of the fifth hundred cases) that of a man 66 years old, with a mature cataract, healing was delayed, but vision was 20/20. Faint opacities of the hyaloid membrane and of the vitreous developed, and the retina was detached one year later.

Retinal detachment is a complication which is often attributable to loss of vitreous with the intracapsular operation. In this series loss of vitreous occurred in only one case; the amount lost was small, and unless it increased the opacities in the vitreous it could not be regarded as a factor. In this case the detachment occurred two months after operation, which is a short time. In the other cases the period from the operation to the onset of the detachment was one year, one and one-half years, two years, one year and one year, respectively. The condition found present in all the cases was opacities of the vitreous, and I believe that this condition, which was possibly due to a low grade cyclitis, was responsible for the detachment. Arruga believes that detachment occurs more frequently after the intracapsular operation than after the extracapsular operation. I am not prepared to share this view, particularly as detachment of the retina after the extracapsular operation is usually due to too deep discissions, with injury to the vitreous followed by organized bands or adhesions between the vitreous and the retina which lead to retinal detachment. This condition does not exist with the intracapsular operation, and no inflammatory changes

occur in the vitreous after this operation unless vitreous is lost or cyclitis develops.

COMMENT

The complication of the intracapsular operation which may be traced to the operative technic is a severe and definite form of iridocyclitis due to traction on the ciliary body. The greater number of cases of loss of vitreous with its complications can be reduced by better anesthesia and greater experience. Glaucoma is much less frequent than with the extracapsular operation. The question of the relative frequency of detachment of the retina is open. The dire late consequences after the intracapsular operation which have been repeatedly brought forward by some writers cannot be substantiated by facts.

DERMOID CYSTS OF THE ORBIT

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Dermoid tumors of the globe, which are solid formations, are relatively common, whereas true dermoid cysts of the orbit are of the rarest occurrence, probably being rarer than intra-ocular retinoblastoma or sarcoma. The typical location of such a cyst is in the upper temporal quadrant of the orbit, near the lacrimal gland. In this location it is easily diagnosed as a smooth rounded mass, adherent to the periosteum, over which the skin moves freely. Should it be located in the upper nasal quadrant, which seldom happens, it must be differentiated from a cephalocele, which is also exceedingly rare in the orbit. Wherever the location may be, one should consider the possibility of the presence of diverticula extending far into the depth of the orbit, as in cases of cyst of the sacrococcygeal region. Under the title of "Oil Cyst of Orbit," Knapp [1] reported a case of a dermoid in which the wall was found on operation to extend from the conjunctiva back to the apex of the orbit. Its removal was attempted by the osteoplastic operation of Krönlein. The dissection proved so difficult, because of the thinness of the wall of the sac, that a portion of it had to be left. Gifford [2] reported a case of an orbital dermoid with several diverticula, for the removal of which three unsuccessful operations had been performed. He succeeded in destroying the lining of the diverticula by the use of practically pure liquefied tri-chloro-acetic acid, a procedure which he strongly recommended in dealing with offshoots of the main cyst. Palomar Collado [3] described a dermoid cyst of the orbit from which a narrow duct led off and extended through a tiny channel in the external bony wall to a knapsack-shaped diverticulum under the temporal muscle. After a second attempt had been made to remove the cyst the hidden pouch was discovered from the fact that the patient was able by making pressure over the muscle to express sebum from the operative wound. An independent operation was required to remove the diverticulum.

Read at the meeting of the American Ophthalmological Society, Hot Springs, Va., June 3, 1936.

1. Knapp, A.: Arch. Ophth. **52**:163, 1923.

2. Gifford, H.: Recurrent Dermoid Cyst: Successful Treatment with Trichloracetic Acid, Arch. Ophth. **2**:305 (Sept.) 1929.

3. Palomar Collado, F.: Rev. méd. de Barcelona **9**:99, 1928.

When a dermoid cyst is neglected it tends to grow larger, especially at the age of puberty. Lesions in its wall may cause it to become tender and painful. They may cause its clinical aspect to change from time to time and complicate its removal because of the attenuation and brittleness produced by them in its wall.

Fig. 1.—Diverticulum of a dermoid cyst. An enormous number of cross-sections of hairs (*H*) are noted in spite of the fact that there are few follicles in the wall of the cyst. The hairs were probably long and densely matted.

It has fallen to my lot to examine microscopically preparations from the walls of thirteen dermoid cysts of the orbit of various sizes and ages. The first nine presented merely the essential histologic features of a dermoid cyst, namely, an inner lining of epithelium and a wall showing hair follicles, sebaceous glands and, in one instance, sweat glands. The third cyst (fig. 1) was of interest because of a small diver-

ticulum filled with a dense matting of hair. The large quantity of hair was in sharp contrast with the small number of hair follicles in the wall. The reverse was found to be true in several of the cysts, in which there were a small amount of hair in the contents and many follicles in the walls. Apparently, for no known reason, hair in cysts may be long or short, just as on the surface of the body. The content of sebum in each of the aforementioned cysts did not always bear a definite relation to the number of sebaceous glands present. There were instances in which there were a large amount of sebum and a small number of glands. One specimen revealed only an epithelial lining and no dermal structures within the wall, marking it as belonging to the rarest and simplest type of dermoid cyst.

Fig. 2.—The epithelium (*E*) ends at *U*, where it is held in the grip of a mass of giant cells, like a sequestrum. The cellular granulation tissue (*Gr*) of the ulcer has undermined the epithelium. In the deeper layers of the wall there are numerous nodules (*N*) of epithelioid and giant cells.

The tenth, eleventh and twelfth cysts had in common partial loss of the regular epithelial lining, there being instead a layer of granulation tissue containing epithelioid and giant cells, representing an ulcerative process. The granulation tissue of the ulcer in one cyst (fig. 2) undermined the adjoining epithelium, like a serpiginous ulcer of the cornea, and at the same time spread out over its surface. Hairs in two cysts had grown into the deeper layers of the walls, making a picture of ingrowing hairs. At varying depths in the soft degenerated walls of several cysts small groups of giant cells were encountered.

The aforementioned pathologic changes are not uncommon in cases of dermoid cyst elsewhere in the body, especially in the ovary, which is said to be the most frequent site. It is generally agreed that the chief cause of the destruction of the epidermal lining is the increase in the intracystic pressure under the influence of an accumulation of

desquamated epithelium and sebum. According to this hypothesis the epithelium of the distended wall, later the sebaceous glands, and still later the sweat glands, because of their greater depth, undergo pressure atrophy. The specimens confirmed the contention that in all the changes in the wall of a dermoid cyst the epithelium exhibits no tendency to proliferate and replace the defects in its continuity as it does on the

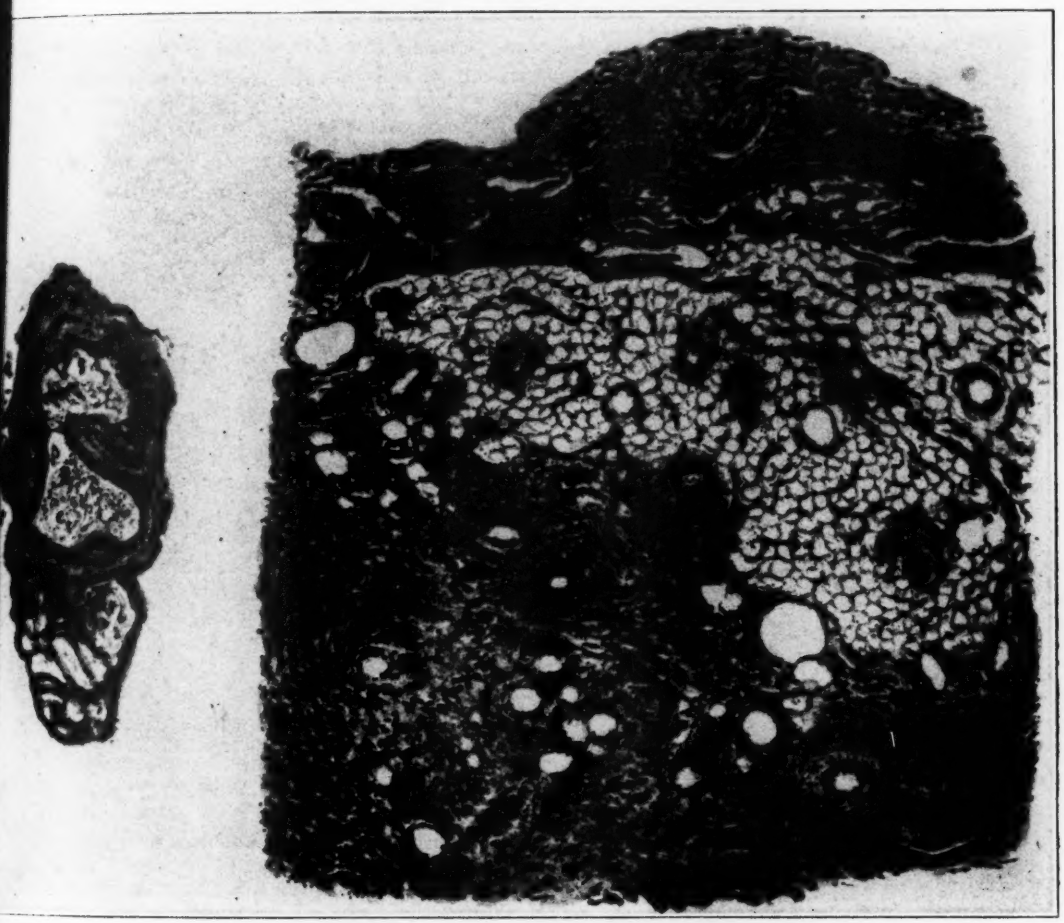

Fig. 3.—Dense granulation tissue is embedded in the subcutaneous fat (*F*) and in the orbicularis muscle (*M*). To the left lies the wall of the dermoid cyst (*W*). In the midst of the granulation tissue there are many cystic holes (*H*) lined by giant cells. The sketch on the side is that of the true cyst (*D*), below which, embedded in granulation tissue (*G*), is the system of adventitious cysts.

surface of the body. As the epithelium disappears the toxic contents of the cyst come in direct contact with the connective tissue of the wall, causing it to produce epithelioid and giant cells as an expression of irritation.

REPORT OF A SPECIAL CASE

The thirteenth cyst observed was in a man 21 years old. Since birth a tumor had been noted at the inner side of the right orbit. It extended superiorly to the angle of the orbit and inferiorly to just beneath the canthal ligament. To the touch it gave the impression of containing a thick fluid. The adjoining orbital wall showed no defect. In removing the cyst a puncture was accidently made in the wall, and an oily fluid came forth containing grayish crumblike particles. At several points the cyst was found to be adherent to the orbital wall. A thin fascia separated it from the orbital fat.

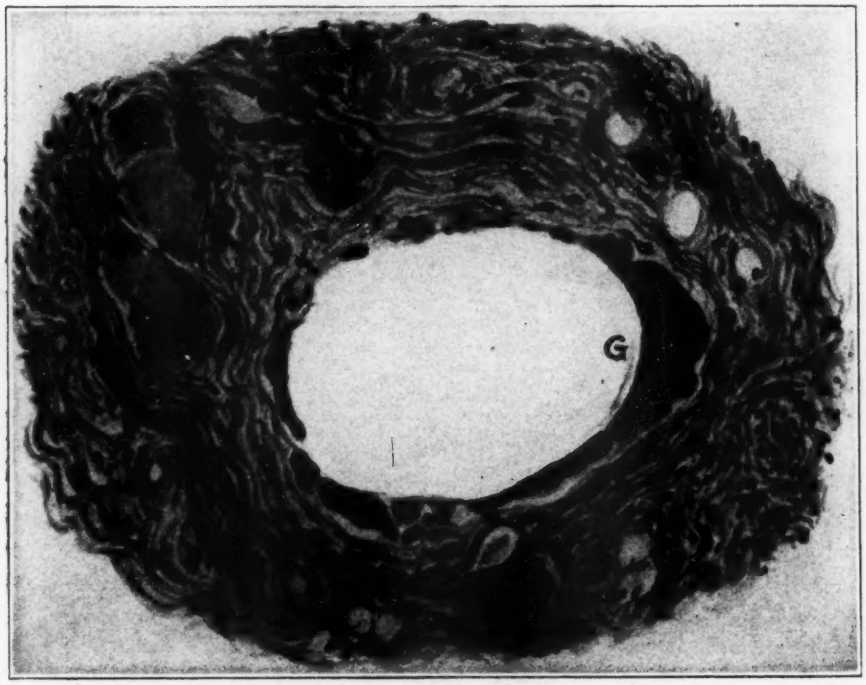

Fig. 4.—A large oval cavity is lined by epithelioid and giant cells, showing a smooth inner contour. To the left are two groups of foreign body giant cells (*F*) enclosing drops of a faintly staining substance (oil). Granulation tissue (*G*) surrounds and separates the spaces.

Microscopic Examination.—Under the microscope the specimen was seen to consist of two parts (fig. 3) separated by a slight constriction. The first part comprised a typical dermoid cyst, and the second part was unlike the first and was evidently of new formation. One portion of the wall of the cyst was composed of almost normal skin containing sebaceous glands and hair follicles. Along another sector the epithelium was missing, and instead a scattering of epithelioid and giant cells was spread over the exposed disorganized stroma.

Of special interest was a third sector of the wall, which was completely transformed into granulation tissue. This new-formed tissue by extending outward and assuming tumor-like proportions formed the bulk of the second part of the specimen. In this way a mass of granulation tissue, large in comparison

with the size of the dermoid from which it sprang, was seen to be embedded in the subcutaneous fat and among the fibers of the orbicularis muscle.

Very striking in the new-formed portion of the specimen was a system of cavities ranging in size from vacuole-like holes surrounded by foreign body giant cells to large cavernous spaces. The inner surface of the walls of the latter (fig. 4) were smooth and were lined by epithelioid or foreign body giant cells. The spaces were in general free from any content, although occasionally a faintly bluish-staining homogeneous substance could be made out. The tissue separating the spaces was dense and revealed many fibroblasts and lymphocytes. The entire formation represented an outspoken inflammatory pseudotumor brought about by the reaction of the tissues to the presence of a foreign substance.

GENESIS OF THE FOREIGN SUBSTANCE

It was evident that the spaces have been occupied by a fatty or oily material that had been dissolved in the fluids used for fixation. Furthermore, the round or oval contour of the spaces spoke for this type of content. It was certain that the oil could have come only from the cavity of the cyst, having been expressed by the high intracystic pressure through the porous granulation tissue that replaced a sector of the wall.

Knapp, in the summary of his case, mentioned that the conjunctiva adjoining the cyst was of a peculiar yellow color and congested. Six months after the operation the conjunctiva still presented the same yellowish discoloration, resembling that of the oily content of the tumor from which he considered it to have been derived. He gave no explanation as to how the oil was expelled from the cavity of the cyst, although he gave a hint by recording the extreme thinness of the wall.

In the literature on the pathologic anatomy of the orbit I have been unable to find any description of spontaneous extrusion of oil from a dermoid cyst of the orbit, although it has been reported by Maresch [4] in cases of dermoid cyst of the ovary and in one case of a dermoid cyst of the testicle. A dermoid cyst of the orbit is superficial, conspicuous and disfiguring and therefore is removed early for cosmetic reasons. Seemingly, because of prompt excision not enough time elapses for the development of sufficient intracystic pressure and toxins to destroy the wall so far as to permit the oily content to escape.

Besides affording interesting anatomic details, the case reported stresses the importance of avoiding a perforation of a dermoid cyst in its removal. If this accident happens, one should be careful not to inundate the wound with the irritating oily material. Finally, the possibility of spontaneous extrusion of oil is to be borne in mind in dealing with orbital dermoid cysts of long standing. In this particular instance

4. Maresch, in Festschrift für Prof. Dr. Han Chiari, Vienna, Wilhelm Braumuller, 1908, p. 36.

it is conceivable that the original dermoid cyst, had it not been excised, might have shrunken owing to degenerative changes in its wall and ceased to exist as such, although the adjoining system of adventitious cysts might have persisted long after, so slowly does the resorption of oil take place.

COMPARATIVE ANATOMY OF THE EYE

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I. THE DEVELOPMENT OF THE ANTERIOR SEGMENT AND ITS SIGNIFICANCE FOR THE DEVELOPMENT OF THE VERTEBRATE EYE AS A WHOLE

The result of an embryologic study of the development of the anterior segment of the eye [1] proved to be of special interest for the evolution of the eye as a whole and gave rise to the conceptions presented in this paper.

The development of the anterior segment of the eye is generally described as follows (fig. 1): The optic vesicle, developing from the neural tube, becomes invaginated. The primordium of the lens, lying in the surface ectoderm, also becomes invaginated; this lens pit deepens, and finally the lens vesicle is separated from the surface ectoderm by mesoderm. In this mesoderm a cleft appears, which is the anterior chamber of the eye.

The process traced was essentially different (figs. 2 and 3): In Torpedo (fish), as soon as the lens vesicle has separated from the surface ectoderm there develops a delicate tissue, nearly cell-free, originating from the cones of the epithelial cells of the optic cup, lens and surface ectoderm. This is the embryonic anterior vitreous body (figs. 2 and 3 *A*).

Von Szily [2] described a similar tissue (*fibrilläres Stützgewebe*) between the germ layers of the young embryo. This observation was confirmed by Studnicka,[3] who created the name "mesostroma." According to this terminology, the anterior vitreous is a mesostroma ecto-ectodermalis (Laguesse [4]), which is a tissue developing between two ectodermal layers and consequently itself of an ectodermal nature. An exactly similar tissue may arise between an ectodermal and a mesodermal layer. The name "mesostroma" has nothing to do with "mesodermal"; the tissue is indifferent.

This paper was read to the O. Z. O. Club of Holland on Dec. 1, 1934.

1. Hagedoorn: (*a*) Nederl. tijdschr. v. geneesk. **71**:460, 1927; (*b*) Brit. J. Ophth. **12**:479, 1928; (*c*) Arch. f. Augenh. **102**:33 and 393, 1930.
2. von Szily: Anat. Anz. **24**:417, 1904; Anat. Hefte **35**:649, 1908.
3. Studnicka: Anat. Anz. **44**:561, 1913.
4. Laguesse: Arch. d'anat. micr. **22**:216, 1926.

In this anterior vitreous in Torpedo a delicate membrane is differentiated, anteriorly marking off the optic cup: the primitive ectodermal cornea (figs. 2 and 3 *A*). The ectodermal character of the primitive cornea in this first stage, so evident in Torpedo, is not so clear in many other animals, in which mesoderm plays its part even in the earliest stages. It is useless to discuss its ectodermal or mesodermal character in these cases (Mann [5]). As will be clear later (experimental embryology), this is not of essential importance. The most primitive process is that in Torpedo, in which the primitive cornea in its first stage certainly develops from the ectoderm solely. By this cornea the eye is

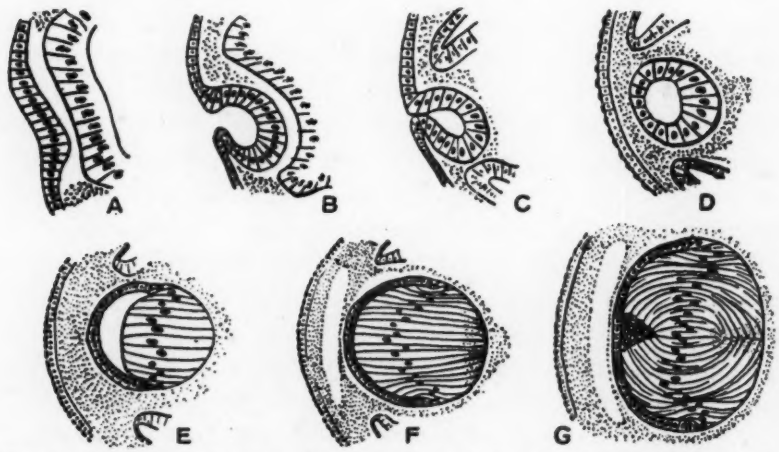

Fig. 1.—Diagrams showing the formation of the anterior segment of the eye as usually described.

marked off in its most primitive form: the primitive eye. The eye never remains at this stage of development. It may reach its ultimate shape along different lines:

1. *The surface epithelium and the primitive eye develop further independently of each other to the skin (or "spectacle glass") and to the definitive eye, respectively, which generally fuse later* (fig. 3 *B, C, D* and *E*).

This is evident in Ammocoetes, the larval stage of Petromyzon (fig. 3 *B*), and still more pronounced in Typhlichtys subterraneus, in which even muscles separate the definitive eye from the skin. This, however, is not the final stage in Petromyzon. In the metamorphosis of Ammocoetes into Petromyzon the eye grows out further, and the skin over the eye changes and becomes transparent. The eye, however, does not fuse with this modified skin but remains separate from it and

5. Mann, I.: Tr. Ophth. Soc. U. Kingdom **51**:63, 1932.

is freely movable (Franz[6]) (fig. 3 *C*). As regards the development of the eye this is a very primitive stage, which is wholly in accordance with the fact that Petromyzon is not rudimentary but primitive in other respects too (Franz). A similar state of development is found in certain amphibian larvae (Bombinator, fig. 3 *D*), in which the already well developed eye lies freely movable under the transparent skin ("Brille spectacle glass"). At first the latter structure is purely ectodermal, consisting of a surface epithelium and a subepithelial cell-free layer (fig. 3 *E*). Soon, however, mesodermal cells grow in, and the mesodermal "glass" is formed. These larvae appear to have free and extensively

Fig. 2.—Photomicrograph showing the primitive ectodermal cornea. A diagram of this stage is shown in figure 3 *A*.

movable eyes fitted with glasses cemented into the skin. A primitive cornea in the purely ectodermal stage is difficult to meet; very soon mesodermal cells grow in (primitive mesodermal cornea).

(This "glass" is something essentially different from an apparently similar "glass" in certain reptilians, which is homologous with the eyelids, as Schwarz[7] proved in Tropidonotus natrix. A "glass" homologous with the eyelids was also found in Misgurnus fossilis by Törö.[8])

As development proceeds the eye becomes united with the "glass" to form the definitive mesodermal cornea (metamorphosis). The course

6. Franz: Zool. Jahrb. (Abt. f. allg. Zool.) **52**:118, 1932; Forsch. u. Fortschr. **8**:383, 1932.

7. Schwarz: Morphol. Jahrb. **72**:499, 1933.

8. Törö: Ztschr. f. Anat. u. Entwcklngsgesch. **98**:97 and 337, 1932.

of this fusion is extensively described for Bombinator by Giesbrecht.[9] In later stages no trace of the dual origin of the cornea can be detected. In Salamandra the construction from the two elements is still very evident, though here, as far as I know, the freely movable eye under a transparent "glass" is not known. In one of my embryologic specimens the primitive cornea, already mesodermal, is clearly marked off from the still totally ectodermal "glass" (fig. 3 *E*). The latter consists of a layer of ectodermal cells (surface epithelium) and a subepithelial

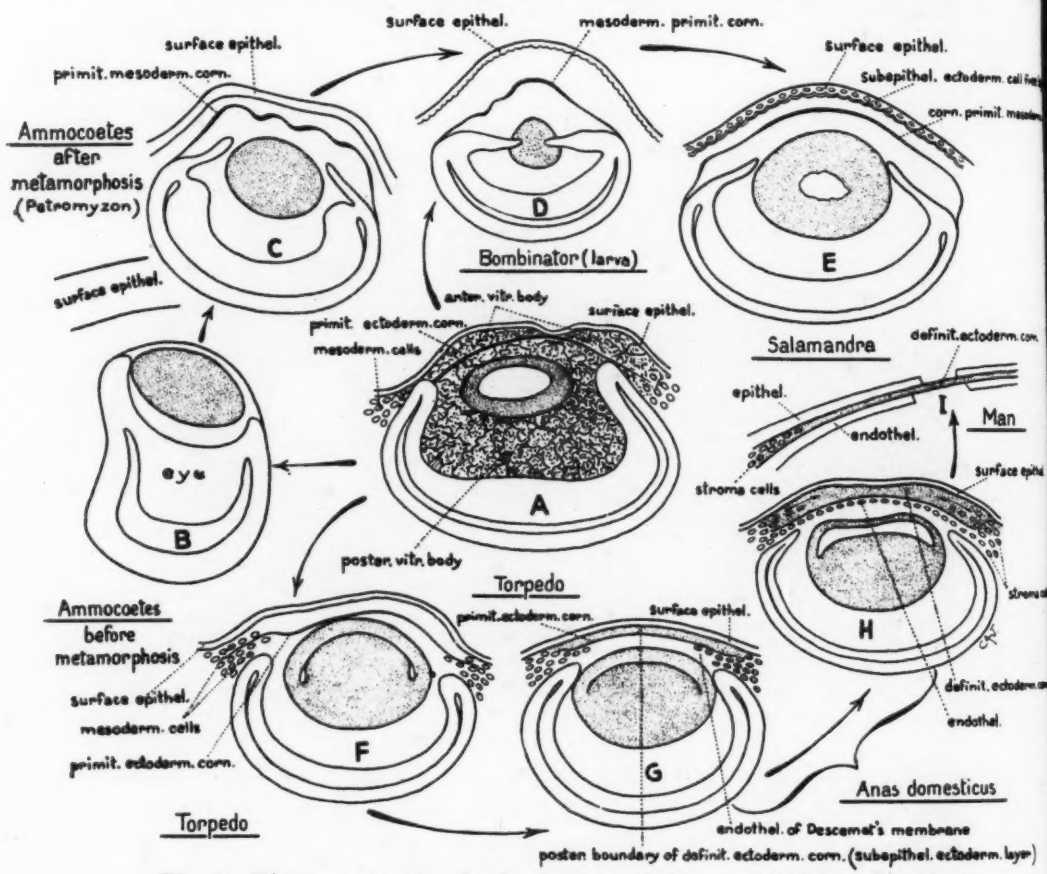

Fig. 3.—Diagrams showing the development of the eyes of different vertebrates.

cell-free layer. This layer has a peculiar structure, clearly showing its origin from about every second epithelial cell. At the periphery mesodermal cells penetrate into this layer.

As will be discussed later, the state in which the eye has not yet fused with its epidermal part marks a very primitive stage, probably the most primitive found in vertebrates. It is interesting that this stage, which is certainly not rudimentary, is present in animals subject to

9. Giesbrecht: Ztschr. f. Zool. **124**:305, 1925.

metamorphosis. With petromyzonts this epidermal part temporarily develops to skin (Ammocoetes, fig. 3 *B*).

2. *The surface epithelium and the primitive eye develop in close contact with each other from the very earliest stages* (fig. 3 *F, G, H* and *I*).

If one studies young stages in Torpedo one finds that the primitive ectodermal cornea just touches the optic cup and is prolonged in the direction of the mesodermal cells (figs. 2 and 3 *A*). In a later stage the primitive cornea, still entirely ectodermal, loses its direct connection with the cells of the optic cup (fig. 3 *F*). In birds the primitive cornea even at its first appearance is separated from the optic cup. It was perfectly described for birds by Knape [10] (*Richtungshäutchen*-"directional membrane") and by Laguesse (*lamelle cornéenne*). A little later lamellae develop under the surface epithelium (as in fig. 3 *E*). The primitive cornea becomes the posterior boundary of this subepithelial ectodermal layer under the surface ectoderm (fig. 3 *G*). The resulting tissue, of course, is ectodermal too and was described by Kessler [11] as the "hyaline layer." According to Laguesse, this layer is not hyaline but lamellar. It is termed here the "definitive ectodermal cornea" (fig. 3 *G, H* and *I*). The first mesodermal element taking part in the structure of the cornea is the endothelium of Descemet's membrane (fig. 3 *G, H* and *I*). Further details will be discussed in a subsequent article on the anomalies of the anterior segment. The further metamorphosis of the definitive ectodermal cornea into the definitive mesodermal cornea occurs as the mesodermal cells grow wedgewise into the preexistent ectodermal tissue (fig. 3 *H* and *I*). That this really is an ingrowth from the corneoscleral border and not a proliferation of cells in the cornea itself is histologically and especially experimentally confirmed by Törö. In marsupial animals this definitive ectodermal cornea is clearly developed, as is confirmed by Keibel.[12] It is also well developed in man (fig. 3 *I*). Those who studied the development of the human cornea chose, of course, the best preserved embryos for their work. However, for the special purpose of demonstrating the definitive ectodermal cornea in man damaged specimens are much better. As this tissue is very resistant the endothelium and epithelium may partly have disappeared while the definitive ectodermal cornea remains intact (fig. 3 *I*). This is the reason why this layer has escaped the attention of other authors. Thus

10. Knape: Mitt. a. d. Augenklin. d. Carolin. med.-chir. Inst. zu Stockholm, no. 11, 1910, p. 105.

11. Kessler: Untersuchungen über die Entwickelung des Auges, angestellt am Hünchen und Triton, Dissert., Dorpat, H. Laakmann, 1871.

12. Keibel: Sitzungsb. d. preuss. Akad. d. Wissensch., no. 20-22, 1928, p. 272.

Fischer [13] speaks of a "cleft" between the endothelium and the epithelium.

Summarizing, both the modes of development—the fusion of the primitive mesodermal cornea with the overlying "glass" or of the primitive ectodermal cornea with the subepithelial layer—are the expression of a developmental phenomenon present in all vertebrates, a process of fusion of the primitive eye with the overlying epidermis.

It is tempting to explain the described process of fusion by the fact that the principal part of the eye develops from the neural tube. The fundamental importance of such a process of fusion, however, seems to be considerably lessened by the fact that the lens develops from the surface ectoderm. Experimental embryology enabled observers to grasp the essential basis of this process, which would have remained hidden to descriptive embryologists.

II. THE CAUSAL DEVELOPMENT OF THE LENS AND OF THE EYE

If in tailed amphibians (Urodela) the lens is extirpated a new lens develops from the iris. Colucci (1891, after Mangold [14]) and, with no knowledge of the previous study, Wolff [15] discovered this fact. This regeneration, however, seems a special feature of tailed amphibians. In anurans, fishes and Lacertilia the potency is very restricted, if present at all. Fischer's [16] case in which a lentoil was found developing between the two layers of the iris in a human eye is important, but up to now no further cases are known. This lentoil showed the same coloring as the lens, a glassy aspect and Morgagni's spherical bodies.

Under normal embryonal conditions there also exists a very close contact between the iris and the lens. In my series this was very evident in Ichthyophis. Treacher Collins [17] and Dejean [18] emphasized the close connection between the optic cup and the lens in studying embryologic material in the common way (*l'assemblage des ébauches de l'oeil*). According to Treacher Collins, the fibers of the zonule develop from this. By a local persistence of this connection certain malformations might be explained. The lens never is stated to develop from the iris under normal embryonal conditions, but Miss Mann did not find a lens in the larval stage of Petromyzon. As Kupffer stated (Hagedoorn [19]),

13. Fischer: Arch. f. Ophth. **126**:504, 1931.
14. Mangold: Ergebn. d. Biol. **7**:193, 1931.
15. Wolff: Arch. f. Entwcklngsmechn. d. Organ. **1**:380, 1895.
16. Fischer: Ztschr. f. Augenh. **69**:30, 1929.
17. Collins, T.: The Bowman Lecture: Changes in the Visual Organs Correlated with the Adoption of Arboreal Life and with the Assumption of the Erect Posture, Tr. Ophth. Soc. U. Kingdom **41**:10, 1921.
18. Dejean: Arch. d'anat. micr. **21**:1, 1925.
19. Hagedoorn,[1c] p. 101.

P. fluviatilis and P. planeri behave differently. Further investigations are necessary. Fischer happened to find that if the lens is extracted from the embryo a small streak of iris tissue is removed with it.

By experiments performed in earlier stages of development a great deal of light is thrown on the essential basis of the development of the lens. After a certain stage the various regions of the early embryo are irrevocably determined to undergo some particular type of development. This mosaic predetermination is demonstrated by numerous experiments in which a region continues its presumptive development even after it has been grafted into an abnormal position. The presumptive eye region of the amphibian embryo has the power of self-differentiation at the early neurula stage.

This primordium ("germ") of the eye behaves as an organizer; later on it induces a lens from the overlying surface ectoderm. In this stage ectoderm from other parts of the body may be substituted. This phenomenon is not restricted to tailed amphibians; most lower vertebrates, even embryos of birds, show it (Reverberi [20]). How general such secondary induction may be in development is as yet unknown (Huxley [21]).

If the ophthalmic vesicle is absent in this period the surface ectoderm does not form a lens independently. Later on only, the surface epithelium also becomes self-determining, so that if the optic cup is removed a lens may develop independently. The cornea probably never reaches a stage in which self-differentiation is possible, which is wholly in accordance with the conception of the development of the anterior segment presented here. Törö [22] even found that the cornea can maintain itself only if there are a normal retina and iris (Salamandra, Axolotl).

Thus the development of the lens is an induction of the ophthalmic vesicle, of the anlage ("germ") of the eye. Consequently the development of the lens from the surface ectoderm is no longer an obstacle to accepting a development of the entire eye from the primordium in the neural tube, followed by a secondary process of fusion with the surface ectoderm.

This process of fusion may fail to occur. If a fertilized ovum is divided into two parts the formative power may be lessened. Under these circumstances the optic cup may develop in the wall of the cephalic vesicle (Schmidt [23]). Moreover, the optic stalk does not appear (fig. 4). If the ocular region of Amblyostoma in the neurula stage is grafted into the abdominal wall, it differentiates there into a more or less well

20. Reverberi: Arch. zool. ital. **16**:480, 1931; Zentralbl. f. d. ges. Ophth. **27**:112, 1932.

21. Huxley, J. S., and DeBeer, G. R.: Elements of Experimental Embryology, London, Cambridge University Press, 1934.

22. Törö: Arch. f. Entwcklngsmechn. d. Organ. **126**:545, 1932.

23. Schmidt: Arch. f. Entwcklngsmechn. d. Organ. **129**:20, 1933.

formed eye. However, this eye likewise lacks a stalk (Huxley). These facts make it probable that the stalk is determined in a relatively later stage, which again is in accordance with the facts given previously, suggesting a secondary process of fusion of the eye (lying originally in the neural tube) with the overlying surface ectoderm.

This most primitive stage which was obtained experimentally, that of an eye still lying in the neural tube, is not met with in the normal anatomy of any vertebrate. Only in the much discussed case of Amphioxus is a comparable condition perhaps present.

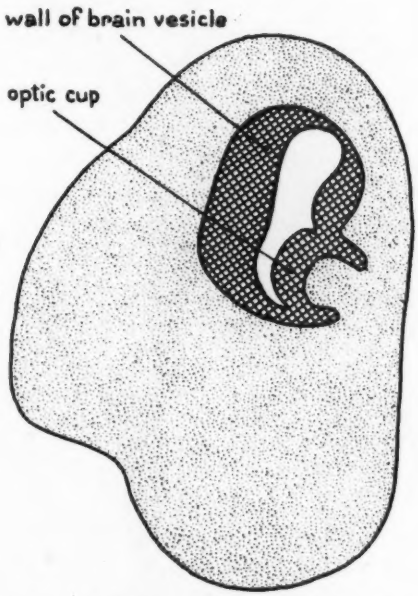

Fig. 4.—Diagram after photograph by Schmidt [23] showing the development of an optic cup in the wall of the cephalic vesicle.

III. THE BRAIN EYE OF AMPHIOXUS: THE "ORIGIN" OF THE EYE IN VERTEBRATES

In Amphioxus an unpaired pigmented area lies in the cephalic vesicle. The lateral eyes of vertebrates cannot be traced here. It is true that this area does not show neurosensory cells, nor can any sensibility to light be detected physiologically. However, pigment from other sources is not present in the brain. Froriep (after Franz [24]) found in the optic pit of the medullary plate pigment which disappears later. Spemann showed that if the portion of the neural tube containing the anlage of the eye is cut into two parts two smaller eyes develop; if one part is too small, clumps of pigmented cells only may be formed.

24. Franz: Ergebn. d. Anat. u. Entwcklngsgesch. **24**:301, 1923.

A very important argument, however, is found in the topography of this area. The terminal nerve enters the brain of Amphioxus in a region analogous to the recessus praeopticus and postopticus in craniotes. Here the optic vesicles develop in vertebrates, which are lacking in Amphioxus. It is true that there is a tendency to believe that the eyes develop from two separate anlagen (Mangold), but in a very early stage of development this double character is less evident and still subject to discussion, as the areas of induction overlap considerably. De Vries,[25] studying congenital malformation, accepted a single primordium of the eye. According to Kupffer (cited by Franz [24]), the anlage of the eyes in Petromyzon would be single.

Adelmann showed that if portions of the eye are grafted with the primitive gut roof (for further details see Mangold and Huxley), the latter reenforces the eyeforming potencies of the lateral portions of the ocular area and further leads to the formation from median pieces of this area of two eyes with optic stalks separated by a region of the floor of the brain representing the optic chiasm, whereas similar pieces without gut roof produce a single eye. Gut roof acts as an organizer for the most important parts of the embryo.

Thus the pigmented area in the cephalic vesicle of Amphioxus may be homologous with the retinal pigment in vertebrates.

There are many authors who do not consider Amphioxus as directly related to the vertebrates, though it is considered to have developed from the same ancestry—an ancestry in which evidently the brain eye was present.

This and the facts mentioned in the previous sections support the opinion of those who have derived the complicated eye of vertebrates from a simple brain eye as found in invertebrates.

Ray Lankaster and, independently of him, Jelgersma [26] derived the eye of the vertebrates from the brain eye of the ascidian larva, which secondarily grows toward the surface. According to Jelgersma, the lens and the cornea develop secondarily. Transitional stages cannot be found, as animals presenting such stages would have been blind and would have disappeared in the struggle for life. Balfour looked on the optic pit as an original surface area which has become secondarily included in the invaginating neural area. This view was accepted and further elaborated by various authors.

As the neural tube in ascidians likewise develops by an invagination of surface ectoderm (Dawydoff [27]), the stage of the ascidians, according

25. de Vries: Nederl. tijdschr. v. geneesk. **70**:2066, 1926.
26. Jelgersma: Morphol. Jahrb. **35**:377, 1906.
27. Dawydoff: Traité d'embryologie comparée des invertébrés, Paris, Masson & Cie, 1928.

to this theory, has been present in the ancestry of vertebrates, and hence this theory is closely related to that of Ray Lankaster and Jelgersma.

In contradiction to this theory other authors supported the view that the lens is the primary organ of vision, like other placodes of the ectoderm (auditory and olfactory placodes), which is secondarily substituted by an outgrowth of the brain. This theory consequently must be abandoned.

Finally Boveri derived the eye of vertebrates from the eyes in the spinal cord of Amphioxus, a view which was not shared by other anatomists but which, according to Mangold, is probably supported by experimental embryology, the area possessing the potency to form an eye being much larger in earlier stages of development. This was shown by Woerdeman, but the area is never so large as to reach into the area of the spinal cord.[28]

Thus the attempt to trace the most primitive stages of the eyes of vertebrates leads into the territory of the invertebrates, since practically no lower stages of evolution are known within the group of the vertebrates (Amphioxus stands apart). The few less perfectly developed eyes have to be considered rudimentary rather than primitive (Froriep[29]). This is the more remarkable as it concerns an organ which is so very complex.

To an even greater extent interest is directed toward the eyes of invertebrates because in spite of the high complexity of the eyes of vertebrates they possess hardly any new features which are not found in the eyes of invertebrates (fig. 5).

IV. THE EYES OF INVERTEBRATES AND VERTEBRATES

Similarities.—Anatomists have long been astonished to find well developed eyes in invertebrates closely resembling those in vertebrates (fig. 5 *j* and *k*). If structures so similar are found among vertebrates they are usually considered as a proof of interrelation (homologous structures). Although the similarity in ocular architecture between certain invertebrates and the vertebrates is evident, yet anatomists have been able to do nothing with this interesting phenomenon except classify the eyes in such cases as convergent structures. The gulf between vertebrates and invertebrates has seemed so wide that comparison of structures has seemed a gross mistake to conservative authors (Plate, Fortuyn

28. Complete literature can be found in: Plate: Allgemeine Zoologie und Abstammungslehre, Jena, 1924, pt. 2. Eisler, in Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1930, vol. 1.

29. Froriep, in Hertwig, O.: Lehrbuch der Entwicklungsgeschichte des Menschen und der Wirbelthiere, ed. 8, Jena, Gustav Fischer, 1906, vol. 2, no. 2.

Droogleever [30]). The philosopher Bergson,[31] purposely ignoring comparative anatomic principles and overlooking the essential differences between vertebrates and invertebrates, ventured to put forward a theory of relation based on his *élan vital.*

As early as 1865-1866 A. Kowalewsky showed that echinoderms and ascidians develop in the same way as Amphioxus (Dawydoff). His statements have withstood all criticism.

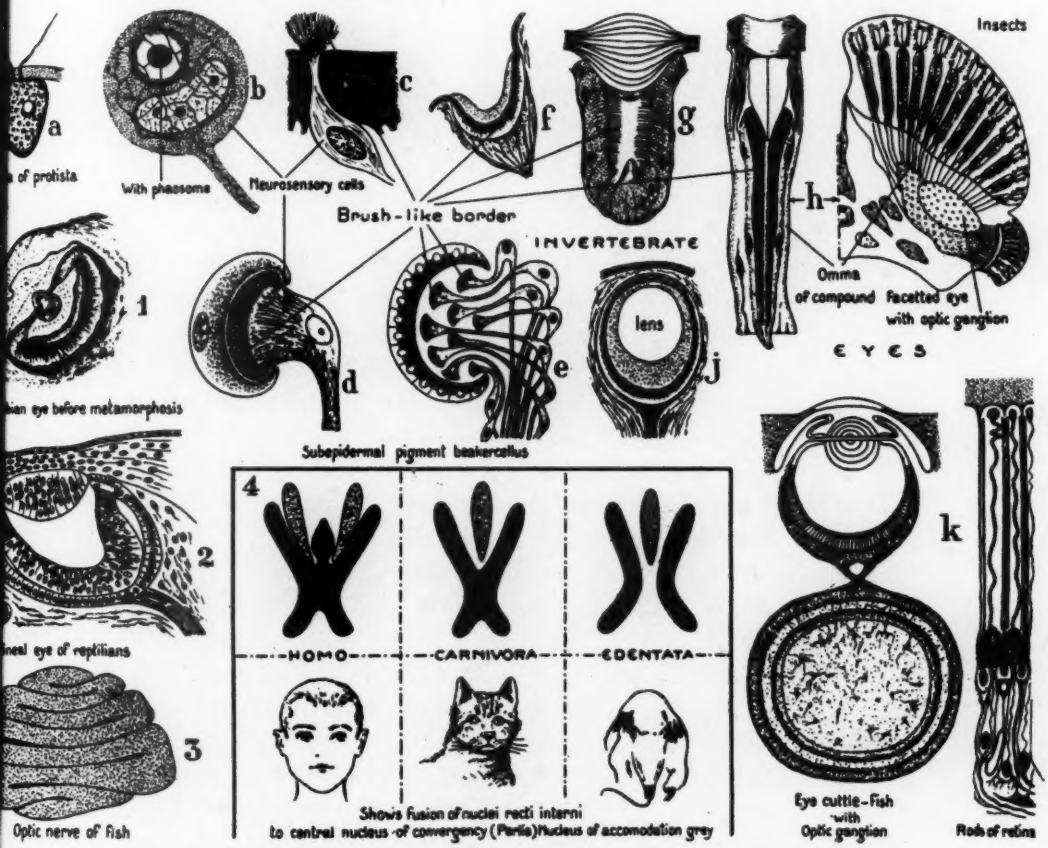

Fig. 5.—Comparison of stages of optic development and of optic elements in invertebrates and vertebrates. Reproduced with permission of Dr. Conrad Berens, New York.

(As Dawydoff remarks, the signs of segmentation are at least very doubtful in ascidians. Perhaps there may be a relation with the fact

30. Droogleever, Fortuyn: Vergleichende Anatomie des Nervensystems, Haarlem, de Erven F. Bohn, 1920, no. 1.

31. Bergson: L'évolution créatrice, Paris, Félix Alcan, 1917.

that the permanent division of the material of the embryo into organ areas appears in a very early stage, very soon after fertilization and even before cleavage.)

In a recent treatise on experimental embryology (Huxley) one is struck by the fact that the material is not subdivided into chapters dealing with vertebrates and invertebrates. General principles govern development in both groups, as signified in polarity, fields and gradients, organizers and the correlation of inner hereditary factors with the outer world. If the causal ontogeny is similar in its principal features, the results, the adult forms, in his case, the eyes of invertebrates and vertebrates, seem to be far more closely related than is suggested by present knowledge of systematic anatomy. This justifies a comparison:

The eyes of invertebrates range from a simple light-sensitive epithelium to the highly differentiated eye of Cephalopodes with a vitreous body, ciliary body, iris, lens, cornea, even eyelids and muscles, closely resembling the eye of vertebrates. The bilateral symmetry found in the eyes of vertebrates by Rabl was described in these cases by Hess (cited by Franz). Between the epichoroid and the vascular layer a silvery membrane is found in certain bony fishes and also in Cephalopodes; it is formed by crystals of guanine.[32] The pupillary reaction, accommodation and muscle function have been studied by physiologists. Only the eyes of insects (faceted eyes, fig. 5 *g* and *h*) follow a different line of development, though the same fundamental common principles are easy to recognize.

It is true that, unlike the evidently analogous shape, the finer histologic details of the sense elements show considerable diversity of structure (Pütter[33]). Though this may be true, all these sense cells are neurosensory cells, which is the essential common feature. This was first recognized by Grenacher and has since been repeatedly confirmed. Grenacher (cited by Fortuyn) stated that the light-sensitive cell is always built after the same scheme, being always a neurosensory cell of ectodermal origin. From this fact Grenacher concluded that as this type of cell is rarely met with in vertebrates the retinal element must be a structure of high phylogenetic antiquity.

Another similarity concerns the structure of the nervous apparatus of the eye, situated on the sense cells in the retina of vertebrates and behind the retina in invertebrates as the sensory cell optic ganglion (fig. 5 *k*). This exemplifies the fact that the relationship of the nervous system of vertebrates and that of invertebrates is much closer than was

32. Duke-Elder, S.: Text Book of Ophthalmology, London, Henry Kimpton, 1932, vol. 1, p. 57.

33. Pütter: Organologie, in von Graefe, A., and Saemisch, E. T.: Handbuch der gesamten Augenheilkunde, Leipzig, W. Engelmann, 1908.

admitted by older anatomists. A review of these common features of the nervous systems in both groups is given in the excellent work of Hanström.[34] Various authors have emphasized the striking similarity of this ganglion in several invertebrates to the structure of the nervous part of the retina of vertebrates. A short description is given by Fortuyn Droogleever in his treatise. Lenhossek studied Cephalopodes, Zawarzin dragon flies, Ramón y Cajal insects. These three authors gave the best studies known on this subject. All three go so far as even to homologize every separate layer of the nervous part of the retina of vertebrates with a layer in the optic ganglion of invertebrates.

Fortuyn Droogleever, however, on the strength of conservative anatomic principles, rejected such comparisons and spoke of convergency. This term "convergency" means only an apparent similarity, simulating a nonexisting relation.)

Perhaps experimental embryology may explain other so-called convergencies within the group of the vertebrates, e. g., that of the auditory organ, as it does not seem necessary that always homologous material should be used by the presumptive ear region. Within the group of man, the so-called convergent features of nonrelated races probably are a result of internal secretion (Bolk and Keith, cited by Ariëns Kappers [35]).

Similar analogies were found in the nervous systems of vertebrates and invertebrates, and the views of those who deny any relationship between those "convergent" structures are not shared by most prominent authors in this field of research.

The separation of the animals into vertebrates and invertebrates, which proved so effective from the standpoint of classification, on the other hand, perhaps was overestimated in its importance for biology as a whole.

Differences Between the Eyes in Vertebrates and Invertebrates.—In considering these two groups of eyes, beside the many similarities, one finds apparently four essential differences:

1. The "gradual evolution" toward perfection in invertebrates; the sudden appearance of a highly developed organ in vertebrates, in which it appears—as expressed by Froriep—like Athena out of the head of Zeus.

2. The complex development of the eye in vertebrates (fig. 5). As is clear from the preceding pages, this view is not right. In vertebrates the eye develops principally from the optic anlage in the medullary

34. Hanström: Vergleichende Anatomie des Nervensystems der wirbellosen Tiere unter Berücksichtigung seiner Funktion, Berlin, Julius Springer, 1928.

35. Ariëns Kappers, C. U.: The Evolution of the Nervous System, New York, Van Riemsdyck Book Service, 1929.

plate which makes the surrounding tissues subservient to its purpose. In invertebrates the development as it is given by descriptive anatomy is also apparently complex. In Cephalopodes the posterior portion of the lens develops from the retina and the anterior portion from the surface epithelium. In Pecten the lens is of ectodermal origin. As far as I know no experiments have been reported regarding these animals with the exception of the work of Ranzi,[36] who succeeded in producing cyclopia in Cephalopodes. Thus it is clear that this "complex development" may no longer be considered as an essential difference.

3. The inverted situation of the sense cells is not an essential difference; it is found also in invertebrates (fig. 5 *d* and *e*). The pineal elements in the eyes of vertebrates are directed toward the light. Weighty arguments, discussed by Franz,[37] speak strongly in favor of the conception that the parietal organ is identical with an eye (fig. 5 *2*).

4. The intimate fusion of the sensory part of the eye and the nervous part in vertebrates whereas these two parts remain separated in invertebrates (fig. 5 *k*). A similar "lack of concentration" occurs in the locomotor system of Cephalopodes, another illustration of the fact that in these animals the nervous system, however highly developed in many respects, is not concentrated to such an extent as it is in vertebrates. The nature of this concentration, evidently indicating that a lying together facilitates cooperation, is expressed for the nervous system by Ariëns Kappers [38] in his theory of neurobiotaxis, which is that the arrangements of the nervous system are caused by the impulses that act in it.

V. NEUROBIOTAXIS

In sharks the abducens nucleus receives its principal impulses from the dorsally situated fasciculus longitudinalis posterior. In bony fishes it receives its principal stimuli from the fasciculus tectobulbaris, which is situated ventrally. Now it appears that the abducens nucleus lies dorsally in the first case and ventrally in the second case.

Numerous similar observations could be made by Ariëns Kappers and his collaborators. An illustrative case of special interest for the ophthalmologist was published by Brouwer (fig. 5 *4*). As with the more frontal position of the eye convergence becomes possible, part of the nuclear cells of the recti interni separate from the rest to form the central nucleus of Perlia in higher vertebrates (carnivores). In anthropoid apes and man the nucleus of Perlia is found in a more frontal region,

36. Ranzi: Atti d. pontif. Accad. d. sc. Nuovi Lincei **82**:74, 1929.

37. Franz: Ergebn. d. Anat. u. Entwcklngsgesch. **24**:293, 1923.

38. Ariëns Kappers, in Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932, vol. 1, p. 45.

between nuclei of accommodation of Edinger and Westphal. This frontal movement of the nucleus of Perlia is, according to Ariëns Kappers' theory, an expression of the fact that convergence is closely associated with accommodation in the latter animals.

Another example of neurobiotaxis given by Ariëns Kappers and of special interest here is the following: In vertebrates the placode (epithelial surface area containing the sense cells) of the organ of smell is situated in the surface epithelium. Under neurobiotactic influence the frontal part of the cephalic vesicle grows out toward this organ of smell. That in embryonic development a neurobiotactic or trophic influence really exists is confirmed by experimental embryology. Burr transplanted an olfactory placode to another region of the head and saw the hemispheric wall grow out toward the transplanted placode. Ariëns Kappers further drew my attention to the fact that the foregoing observation is also confirmed in cases of arhinencephaly. It is interesting to note that the sense cells do not move in the direction of the brain but the brain in the direction of the sense cells, which fact, as well as the congenital deformity, emphasizes the great importance of these sense cells for the vertebrate body.

The function of the organ of sense is a result of the cooperation of sense cells and neurons. In vertebrates all neurons are originally incorporated in the neural tube, and consequently the primordia of the nervous parts of the organs of sense are situated there as well. In the case of the organ of smell this necessitates the described process of outgrowth of the forebrain toward the placode of sense cells in the skin. In the case of the organ of sight the nervous part of the organ is likewise situated in the neural plate, later in the neural tube. However, there is an essential difference from the organ of smell. Whereas the placode of the organ of smell lies outside and remains outside of the area involved in the closure of the neural crests, the placode of the organ of sight is located in this area and therefore is involved in the closure of the neural tube. It is much easier for the cells of the nervous part of the eye to follow neurobiotactic influence, and thus the situation of the nervous part of the retina directly on the sensory part ranges harmoniously between the various other examples of neurobiotaxis.

(The embryonic optic nerve contains a great number of cells. In many cases in embryonic life a migration of nerve cells is found. Now it seems interesting to know whether in vertebrates the brain part of the retina migrates toward the interior of the eye or whether it is situated there from the beginning. I believe that this has not yet been investigated. However, experiments seem to show that complete eyes—though the optic stalk may not develop—including the brain part, develop from transplanted optic vesicles, so that in this stage at least the greater

part of the nervous system of the eye must be already present. Thus the numerous cells found in the embryonic optic nerve must be glia cells.)

Now the third essential difference will be considered again:

VI. THE GRADUAL EVOLUTION OF THE EYE IN INVERTEBRATES AND THE SUDDEN APPEARANCE IN VERTEBRATES

With this formula I do not want to support a theory of evolution, but this is the briefest way to express that in invertebrates one finds all stages of evolution of the eye from the simple sense cells in the surface ectoderm to the highly developed eyes of Cephalopodes, whereas among the vertebrates even the very poorly developed ones already possess highly developed eyes.

The first fact, that of the gradual evolution in invertebrates, needs no further explanation, as it ranges harmoniously among many other facts in anatomy. Within the group of the vertebrates transitional stages between lower forms and mammals are found (e. g., the auditive organ) which give further evidence of a relationship between those creatures marked by the common feature of a vertebral column. These facts are the basis of anatomic classification; furthermore, they suggested the theory that present living organisms developed from ancestors possessing features of present-day lower forms. This theory is supported by the fact that embryonal stages of lower vertebrates are met with in the course of development of higher forms (von Baer's law). Modern authors not seldom come to an opposite conclusion (Franz [39]): *"Phylogenie ist Oontogenie"* (compare Aschoff [40]). The facts on which this theory is based must be the result of common developmental processes, the existence of which is directly demonstrated by experimental embryology. They are primary features of protoplasm, active in creating a more ideal morphologic substrate for functions already present in the protoplasm of the most primitive monocell. Thus appear similar embryonal stages (blastula, gastrula, germ layers) and similar adult forms (nerves, muscles, gut, eye). From this point of view the eye of vertebrates is a more perfect manifestation of potencies evident also in the eye of invertebrates. If, nevertheless, the problem of the "sudden appearance" is put, this general point of view is left behind, and a question is raised concerning the special development of vertebrates. By considering facts of descriptive anatomy in the light of developmental principles detected by experimental embryology I shall try to

39. Franz: Ontogenie und Phylogenie, Abhandlungen zur Theorie der organischen Entwicklung, Berlin, Julius Springer, 1927, no. 3.

40. Aschoff, Ludwig: Ueber die Stellung der Naturwissenschaften zur Religion, Zeitwende, no. 2, February 1927.

trace the way in which protoplasm strives to higher morphologic differentiation, culminating in the developmental processus of vertebrates. The combined inner factors—polarity, gradients, transmissive and transportative influences (Child [41])—governing this morphologic differentiation will be called "the field":

The protoplasm grows or strives toward a morphologic differentiation facilitating and perfecting its essential functions. In the monocell this process is soon terminated by cell division leading to a production of new monocells. Thus in one cell a high standard of morphologic differentiation is not known, is hence impossible and therefore differentiation is not checked or retarded but limited, though the potency may be present (fertilized ovum of vertebrates). These monocells may be called individuals of the first order.

In the multicellular individual the first step, cell division, occurs as well; the next step in the monocell, cell separation, however, does not follow. Bolk [42] pointed out the fact that the adult human body shows many features characteristic of the fetus of the ape. Thus, compared with the development of the ape, the development of the human body in these respects is less advanced, checked, conservative (Bolk); the development of the ape is more progressive, propulsive (Bolk). Following Bolk's line of thought, protoplasm develops propulsively in the monocellular and conservatively in the multicellular individual. The cells of the multicellular individual thus keep together; the influences indicated as "the field" assume a new shape; a common field of the second order appears, governing the development of the multicellular individual as a whole. This field checks the influence of the individual fields of the cells striving to universal morphologic differentiation, resulting in a retardation of universal but a stimulus to subsequent partial, specialistic morphologic differentiation. Thus cell division for purposes of multiplication only is made subservient to higher morphologic differentiation of the multicellular individual, an individual of the second order. However, this morphologic differentiation is rather restricted if the potency of reproduction is maintained in the cells sharing in the architecture of the multicellular individual. Here—as in monocells—in the adult animal a new independent field appears, governing the development of a new individual: bud formation. A process of retardation, the appearance of sex cells (with completely retarded morphologic differentiation and a totally independent individual field) enables a higher standard of morphologic differentiation, the other cells exclusively serving the morphologic differentiation of the individual.

41. Child: Arch. f. Entwcklngsmechn. d. Organ. **117**:21, 1929.

42. Bolk: Das Problem der Menschwerdung, Jena, Gustav Fischer, 1926; Proc. Roy. Acad. Amsterdam **29**:3, 1925.

It is doubtful whether there is already a most primitive organ of vision possible in the organization of the individual of the first order (stigma of protists, fig. 5 *a*). In the individual of the second order a well developed eye may be present, even with a lens, so that in this stage of morphologic differentiation of the protoplasm in general the principles of the specialistic morphologic differentiation of the eye present in vertebrates are already reached.

In the individual of the second order the cells or groups of cells governed by a local independent field develop to (generally) independent

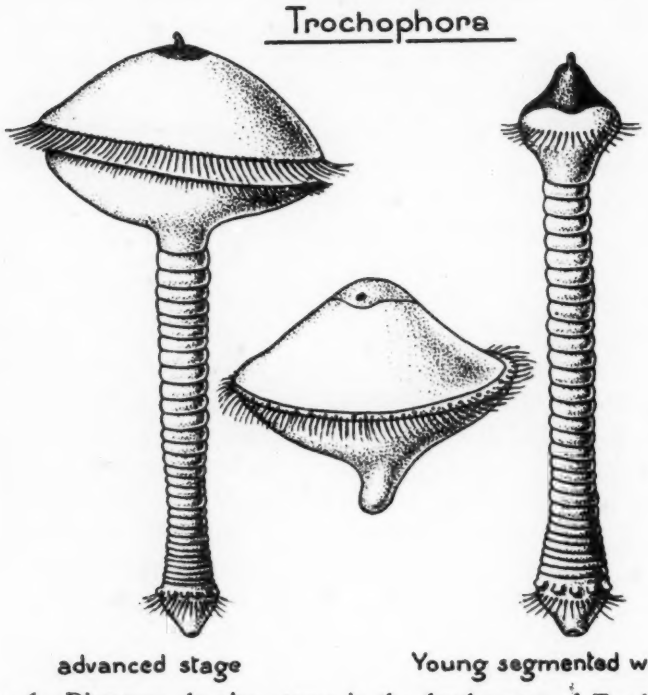

Fig. 6.—Diagrams showing stages in the development of Trochophora.

individuals, which (may) separate from the mother animal. This separation may not occur, so that the development compared with that of individuals of the second order is conservative. In lower forms—in analogy with bud formation—the individual of the second order must grow to full size (Trochophora larva, fig. 6) before the formation of new independent fields becomes manifest, governing the differentiation of the segments. As the segments develop, the influences indicated as the fields assume a new shape focusing in the head region—the original trochophora—govern the development of a homonymously segmented animal. This field checks the influences of the fields of the second order striving to universal morphologic differentiation, resulting in a retarda-

tion of universal but a stimulus to specialistic development in many respects opposite to that of the trochophora, the head region. Morphologic differentiation is limited in the individual of the second order. By a conservative behavior, a "keeping together," the way toward higher morphologic differentiation of protoplasm is opened. The stronger the retardation of the morphologic differentiation under the influence of the fields of the second order the more perfect is the morphologic differentiation of the whole. Thus the appearance of independent fields in individuals of the second order for the purposes of multiplication only is made subservient to higher morphologic differentiation by conservativisim and retardation. The fields of the individual seem to focus in the head region (dominant region—Child). These segments may be capable of living independently (proglotiddes of taeniae). As the field of the third order seems to attain its full development only after the appearance of the segments it secondarily may disturb the morphologic differentiation governed by fields of the second order and induce a new field under its influence. It seems in many heteronymously segmented animals as if a process of temporary decentralization into segments (homonymous larva) is followed by a process of rebuilding and concentration.

In vertebrates this apparent temporary decentralization into segments is overshadowed by the temporary decentralization in organ primordia (with their local fields), a manifestation of the strongly developed field of the third order in vertebrates. Probably here, likewise, retardation of the morphologic differentiation by these local fields favors a more ideal arrangement and association (e. g., neurobiotaxis). All the same the first process—the temporary decentralization in segments—is present; the local fields still develop into segments. However, this development is checked, retarded, especially in higher vertebrates. Secondarily these segments develop or are rebuilt under the influence of the field of the third order, for instance, to an extensional growth of the head region, the anterior part of which is not segmented and comparable with the trochophora of segmented invertebrates. This conclusion is fully in accordance with modern views on the "origin" of the head region in vertebrates (Matthes,[43] Bystrow[44]). According to these authors, the head region consists of an anterior nonsegmented "phylogenetically older" part and a posterior "phylogenetically younger" part, derived from assimilated segments.

The morphologic differentiation induced by a field of the second order may already produce eyes similar to those in vertebrates. Hypo-

43. Matthes: Ergebn. d. Anat. u. Entwcklngsgesch. **23**:669, 1921; **24**:142, 1923.

44. Bystrow: Ztschr. f. Anat. u. Entwcklngsgesch. **100**:363, 1933.

thetically, most primitive vertebrates therefore might be expected to have had eyes even in a stage resembling the gastrula or the trochophora. For this reason it seems very comprehensible that the present lowest vertebrates, so much further metamorphosed, already possess well developed eyes.

In the foregoing consideration the head region was considered the primary region. This is in accordance with the theories of Hubrecht, Keibel and others (compare Spitzer [45]), who described the head region as originating from the gastrula, followed by a secondary process, the development of a trunk and tail. De Lange [46] recently came to a similar conclusion. According to the recent theory of Spitzer,[45] the segments of the vertebrate body develop by repeated budding (*Geschwistermomonten*) and hence are considered individuals of the second order. This reminds one of the old theories of Haeckel, Oken, Owen and Goethe. Both views are in accordance with the conclusion I have given. This conclusion supports the theory of Plate and Studnicka, who derived the eyes of vertebrates from those in the trochophora larva and considered both the parietal and lateral eyes.

The fact that the eyes in very primitive stages of vertebrates must have had a relatively very advanced development probably accounts for the fact that the optic field is more extensive than the region which in normal development actually gives rise to the eyes (Woerdeman).

It is probable that this very early appearance in still crudely common stages, before the evident branching of morphologic differentiation develops, accounts for the fundamental similarity of the organs of light perception in the living world. Such an organ behaves like a living element of protoplasm. If this view is right one may expect that the eye, acquiring its chief morphologic characteristics already in the "premetameric stage," will show some features in its architecture reminding one of invertebrates.

This indeed is evident from the following facts:

1. The sense cells of the eye are neurosensory cells not only in invertebrates, in which these cells are common, but also in vertebrates, in which they are extremely rare and otherwise are found only in the organ of smell, the saccus vasculosis and the ependyma. Several sensations, such as taste, touch and that of equilibrium, which in invertebrates are perceived and conducted by neurosensory cells, are conducted by neurons in vertebrates, in which only vision and olfaction are perceived by neurosensory cells.

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45. Spitzer: Ergebn. d. Anat. u. Entwcklngsgesch. **30**:1, 1933 (p. 120).

46. de Lange, D.: The Head Problem in Chordates, J. Anat. **70**:515 (July) 1936.

2. There are present in the retina peculiar amacrine cells, which are very common in invertebrates but rare in vertebrates. In amacrine cells no difference between their various offshoots can be observed, in which they resemble the primitive ganglion cells. Such cells are found only in the tectum of fishes and in the olfactory bulb of Amblyostoma. Cajal considered the amacrine cells of the retina to conduct asynaptically, thus absolutely identifying them with primitive ganglion cells.[47]

3. There is a peculiar connective tissue of the vitreous body (mesostroma), similar to embryonal tissue (von Szily, Studnicka, Laguesse) and to tissues in adult invertebrates but without an analog elsewhere in adult vertebrates. Only in the tail of tadpoles is a similar tissue present elsewhere in vertebrates.

4. The sphincter of the iris develops apparently from brain tissue.

5. The muscles of the iris apparently have no nervous supply (Franz). In other vertebrates the arrangement of the eye in the vertebrate body is more completed, which is manifested in a central nervous supply of the inner ocular muscles. Even in amphibians, however, the eye has an independent reaction to light.

6. Perhaps with the exception of the ocular muscles no sign of a metameric origin of the eye was ever detected; there is no sign of a rebuilding from segmented material.

In the light of these facts the "sudden appearance" of the eye in vertebrates is comprehensible, this being the result of its relatively early morphologic differentiation ("high phylogenetic antiquity"), as Grenacher emphasized for its principal constituent element, the neurosensory cell.

In vertebrates the primordium of this eye is situated in the neural tube. Neurobiotactic influence causes the nervous apparatus to be connected with these sense cells. This complex eye secondarily becomes connected with the surface ectoderm by a process described in the beginning of this paper.

47. Cited by Ariëns Kappers.[38]

BILATERAL METASTATIC CARCINOMA OF THE CHOROID

SUCCESSFUL ROENTGEN TREATMENT OF ONE EYE

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AND
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Choroidal metastasis of carcinoma is still rare, according to published reports. Statistics as to the relative frequency of metastatic carcinoma of the choroid are notoriously unreliable, since they represent one man's or one clinic's experience only. Thus, Uhthoff [1] gave the ratio of patients with this condition to patients with ocular conditions as 1 : 30,000, while Sattler [2] reported a ratio of 1 : 300,000. Stallard [3] reported 6 cases described in the records of Moorfields Hospital, a ratio of 1 : 147,000. It has been suggested that the condition is much more frequent than has been reported, since such metastasis must occur often in terminal stages of carcinomatosis and therefore be overlooked. Against this suggestion is Michaïl's [4] report of 1 case of this condition in 48,000 eyes examined microscopically. However, reports of cases are becoming more frequent. Whether this represents an actual increase of the incidence of choroidal metastasis, better medical observation or simply more interest in the subject is, of course, undeterminable. We shall allude further to this increase.

Statistics are also at variance as to the exact number of cases reported. DeLong [5] in 1933 stated that he had found reports of 135 cases in the literature, while Hudson [6] in 1934 gave the figure as 149. The most accurate and exhaustive treatise found by us is that of Ask,[7] in which he tabulated and analyzed 211 cases of uveal metastasis of carcinoma to Oct. 10, 1934, including 1 new case. In 59 of these the diagnosis was not proved by pathologic examination, and in the remain-

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Read at the meeting of the American Ophthalmological Society, Hot Springs, Va., June 2, 1936.

1. Uhthoff, W.: Deutsche med. Wchnschr. **30**:1423, 1904.
2. Sattler, H.: Die bösartigen Geschwülste des Auges, Leipzig, S. Hirzel, 1926, p. 221.
3. Stallard, H. B.: Proc. Roy. Soc. Med. **26**:1042, 1933.
4. Michaïl, D.: Ann. d'ocul. **169**:119, 1932.
5. DeLong, P.: Am. J. Ophth. **16**:712, 1933.
6. Hudson, A. C.: Proc. Roy. Soc. Med. **27**:304, 1934.
7. Ask, O.: Acta ophth. **12**:308, 1934.

ing 152, 7 patients were stated to have metastasis in the iris and ciliary body only, leaving a total of 145 cases of choroidal metastasis proved by histologic study. There are at least two duplications in Ask's list, one of Greenwood's cases (no. 124) being the same as Greenwood and Southard's case (no. 57), and one of Moore and Stallard's cases (no. 208) being the same as an earlier case of theirs (no. 192). Ask did not include the case of Suker and Grosvenor [8] among the cases in which the diagnosis was proved, but we feel that it should be accepted, although the specific type of tumor is not mentioned. We have collected, in addition, 12 instances in which the diagnosis has been proved, which, with our case, make a total of 156. We have also found 1 additional case of metastasis to the ciliary body.

Smoleroff and Agatston [9] reported 1 case in which the patient presented the extremely rare picture of metastasis to the retina without choroidal involvement. This should probably be included in the group reported, since the condition represents the same mechanism of metastasis.

There are, then, 156 proved cases on record of metastatic carcinoma of the choroid, 8 in which it was present in the iris and ciliary body only and 1 in which the retina only was involved. In addition to Ask's 58 cases (Suker and Grosvenor's case added to the proved cases), we have collected 6 instances in which a microscopic diagnosis was not made, making a total of 229 cases of uveal metastasis.

Ask drew some interesting comparisons between the location of the primary tumor producing uveal metastasis and the relative frequency of this tumor among all types of carcinoma. Thus, carcinoma of the breast is responsible for 50 per cent of uveal metastasis but has a relative frequency of only 13.5 per cent. Carcinoma of the stomach, with a relative frequency of 36.5 per cent, produced only 3.3 per cent of the uveal metastases. Ask demonstrated by strictly statistical methods that carcinoma in certain primary sites—the breast, bronchi and lungs, and prostate—tends to produce uveal metastases, while in other sites—the stomach, uterus and ovaries, and skin—it has the opposite tendency, and concluded that the cause of this is the difference in the tendency of the various types of carcinoma toward hematogenous metastasis, rather than differing affinities for uveal tissues.

It seems to us, however, that this is insufficient to account for the frequency of choroidal involvement as compared to that of comparable tissues, when the distribution of the ophthalmic artery is considered.

8. Suker, G. F., and Grosvenor, L. N.: Ophthalmology **5**:580, 1909.

9. Smoleroff, J. W., and Agatston, S. A.: Metastatic Carcinoma of the Retina: Report of a Case, with Pathologic Observations, Arch. Ophth. **12**:359 (Sept.) 1934.

TABLE 1.—*Reported Cases Not Included in or Subsequent to Those in Ask's List*

Author	Sex	Age Years	Location of Metastatic Tumor	Diagnosis		Location of Primary Carcinoma	Other Metastatic Tumors	Comment
				Clinical	Micro-scopic			
Cohen, M.: Arch. Ophth. **54**: 205, 1925*	♀	?	Choroid of both eyes	+	..	Breast	No autopsy or microscopic examination reported	
Weeks: Arch. Ophth. **54**: 205, 1925*	♀	60	? (Choroid from context)	+	+	Lung	.....	Carcinoma of lung observed at autopsy; not recognized ante mortem
Shields, J. M.: Am. J. Ophth. **9**: 541, 1926*	♂	70	Choroid of both eyes	+	..	Brain (?)	No report	
Knapp, A.: Metastatic Carcinoma of the Ciliary Body: Report of a Case, Arch. Ophth. **1**: 604 (May) 1929‡	♀	68	Ciliary body of right eye	+	+	Breast	Mediastinum and left side of chest	Adenocarcinoma of breast and eye
Morgan, O. G.: Am. J. Ophth. **15**: 644, 1932*	♀	36	?	+	..	Breast	No report	
Zentmayer [12] ‡	♀	60	Choroid of both eyes	+	..	Breast	Autopsy refused; roentgenogram shows involvement of lower half of left lung and of liver and spine	Scirrhous carcinoma; radium treatment of eye
Greenwood: Am. J. Ophth. **17**: 348, 1934*	?	?	? Choroid	+	..	Breast	No report	
Heintz: Bull. Soc. belge d'opht. **69**: 25, 1934†	♀	34	Choroid of right eye	+	+	Breast	No report	Atypical "epithelioma" resembling carcinoma of the breast
Hudson [6] ‡	♂	41	Choroid of right eye	+	+	Lung (?)	Autopsy refused	Papilliferous cystadenoma
McDannald, C. E., and Payne, B. F.: Metastatic Carcinoma of the Optic Nerve and Choroid, Arch. Ophth. **12**: 86 (July) 1934‡	♀	42	Optic nerve and choroid of right eye	+	+	Breast	No report	Carcinoma, group III; apparently the optic nerve was involved first

Smoleroff and Agatston[9] ‡....	♂	55	Retina of right eye	+ (chor.)	+	Esophagus	Liver, lungs, adrenal glands, lymph nodes, spine	Alevolar carcinoma; choroid not involved
Goldstein, I., and Wexler, D.: Metastasis in the Choroid from Adenocarcinoma of the Testis, Arch. Ophth. **13**: 207 (Jan.) 1935‡	♂	4	Choroid of right eye	+	+	Testis	Retroperitoneal, cervical and mediastinal nodes; trachea; right bronchus; lungs	Adenocarcinoma
Smoleroff, J. W., and Agatston, S. A.: Two Different Fundus Pictures in Metastatic Choroidal Carcinoma: A Clinicopathologic Study, Arch. Ophth. **14**: 810, (Nov.) 1935‡	♀	?	Choroid of right eye	+	+	Breast	Lymph nodes	Detachment of retina; carcinoma cells in short posterior ciliary artery
Smoleroff, J. W., and Agatston, S. A.: Two Different Fundus Pictures in Metastatic Choroidal Carcinoma: A Clinicopathologic Study, Arch. Ophth. **14**: 810, (Nov.) 1935‡	♀	40	Choroid of both eyes	+	+	Breast	Generalized	No detachment of retina; carcinoma cells in long posterior ciliary vessel
Bloch and Siobrowski: Klin. Oczna **12**: 278, 1934†	♀	48	Choroid of both eyes	+	..	Breast	Left axilla; humerus	
Venco, L.: Ann. di ottal. e clin. ocul. **63**: 401, 1935†	♂	50	? Choroid	+	+	Thyroid	No report	
Knapp, F. N.: Am. J. Ophth. **18**: 371, 1935*	♂	39	? Choroid	+	+	Lung	No report	
Orth, H.: Klin. Monatsbl. f. Augenh. **95**: 675, 1935†	♀	?	? Choroid	+	+	Breast	Lung	
Kahoun: Českoslov. oftal. **2**: 107, 1935†	♀	55	Choroid of right eye	+	+	Breast	No report	Metastasis to choroid, retina and optic nerve 8 yr. after primary carcinoma
Köppl, I. F.: Klin. Monatsbl. f. Augenh. **95**: 310, 1935†	♀	?	Choroid and iris of both eyes	+	?	Bronchus	No report	

* Data from report of society transactions.
† Data from abstract of original article.
‡ Data from original article.

This vessel arises from the internal carotid artery at a right angle, gives off the central artery of the retina at a right angle, the lacrimal artery at nearly a right angle, the posterior ciliary arteries at oblique angles, the much larger supra-orbital branch at about a 45 degree angle and, after giving off the ethmoid arteries at nearly right angles, divides into the frontal and medial palpebral arteries. Granting that carcinoma of the breast has a great tendency to metastasize hematogenously, this would seem only to increase the probability of cells entering the ophthalmic artery. From the purely mechanical standpoint, there seems to be no reason why the other branches, particularly the supra-orbital and terminal branches, should not receive some of the emboli. Also, there seems to be no reason for the low incidence of uveal metastasis outside the choroid.

Only one explanation seems to fit all the facts. Carcinoma of the breast tends toward hematogenous metastasis, releasing comparatively large numbers of cells into the circulation. A certain proportion of these cells find their way into the ophthalmic artery and are distributed to the tissues supplied by it. Those which reach the choroid through the posterior ciliary arteries and, to a less degree, those which reach the iris and ciliary body through the anterior ciliary arteries find nutritional conditions suitable and grow; elsewhere they perish. The difficulty of entrance into the ophthalmic artery may partly account for the low frequency of ocular metastasis. In other words, we are postulating a specific affinity of uveal tissue, particularly the choroid, for cells from carcinoma of the breast.

In the total series, metastasis was bilateral in 20.8 per cent—surely too large a percentage to be explained on grounds of mechanics and probability but logically explainable by the release of a shower of cancer cell emboli, which are distributed through the entire circulation and grow only in the location where nutritive conditions are right. It is possible that anomalies in the course of the ophthalmic artery might be a factor.

A further point of interest is the incidence of pulmonary metastasis. In the complete series of 221 cases only 59 autopsies were reported. Among these cases, pulmonary metastases were found in 42; reports were indefinite in 5, and pulmonary metastases were absent in 12. Considering those patients as showing metastasis for whom indefinite reports were made, the percentage of pulmonary metastasis in patients who came to autopsy is 83. One would naturally expect a larger percentage, in view of the impossibility of lymphatic extension to the eye. The absence of pulmonary metastasis in 17 per cent can be accounted for only by failure to observe very tiny nodules, or by cancer cell emboli passing through the lung without lodging there. The latter explanation

is probably the correct one, in view of MacCallum's statements: "We must assume that the floating cells have passed through wide capillaries of the lung to reach the other organs" [10a] and "There is no difficulty in accepting the idea that the tumor cells may slip through the lungs, for in many cases they are not much larger than the blood cells and ought to pass readily." [10b]

The increase in the reported cases, which has already been mentioned, is shown in table 2, which is based on Ask's and our figures.

TABLE 2.—*Data Showing Increase in Reported Cases of Metastatic Carcinoma of the Choroid*

Date	Number of Cases	Cases per Year (Average)
1872 to 1899, inclusive (first case reported by Perls in 1872)....	36	1.3
1900 to 1909, inclusive.....	47	4.7
1910 to 1919, inclusive.....	32	3.2
1920 to 1929, inclusive.....	62	6.2
1930 to 1935, inclusive (6 years).....	53	8.8

REPORT OF CASE

Clinical History.—Sister M. U., aged 72, was admitted to the St. Joseph Hospital on March 28, 1930, complaining of shortness of breath on exertion, headaches and vertigo. Except for pneumonia followed by jaundice in 1927 and chronic sinusitis, her past history was essentially irrelevant.

On physical examination carcinoma of the right breast was discovered, with metastases to the axillary nodes. The blood pressure on admission was 136 systolic and 65 diastolic but ranged as high as 185 systolic and 88 diastolic. On April 7 radical amputation of the right breast was performed by Dr. J. O. Skinner. Microscopic examination (fig. 1) on April 30 (Dr. R. Koritschoner) showed infiltrating carcinoma simplex.

On June 10, 1930, cholecystectomy was performed by Dr. Skinner.

On Oct. 22, 1933, the patient was readmitted with the same complaint as before and, in addition, cough associated with pain in the left side of the chest. No râles or rubs were heard by means of the stethoscope. The report on a roentgenogram taken on November 11 stated that the pulmonary field was clear on the right side. On the left side there was uniform shading of the base of the lung, including the lower lobe. It was thought that this might be the result of the pneumonic process or might be due to pleurisy of malignant origin. A clinical diagnosis of pulmonary metastasis was made at this time.

On December 21 no change was found.

On May 8, 1934, the patient was readmitted to the hospital because of pain in the left side, which was more severe than before, harsh cough, dyspnea, nausea and vomiting. At this time she first began to complain of pain in the left eye and orbit. Small hard preauricular glands were palpable. There were small nodules in the scar resulting from amputation of the breast and a small nodular mass in the subcutaneous tissue of the right lower abdominal quadrant. There was also a nodule in the scalp. Roentgenology at this time revealed no change in the picture of the chest from that of the previous examination.

10. MacCallum, W. G.: (*a*) A Textbook of Pathology, ed. 4, Philadelphia, W. B. Saunders Company, 1928, p. 1117; (*b*) p. 1118.

From this time on the course was slowly downward, punctuated by asthmatic attacks. At no time was there marked cachexia, but a steady gradual weakening was noted. The subcutaneous metastatic tumors did not enlarge noticeably. Roentgenograms of the chest taken as late as Sept. 6, 1934, still showed no change. About November 1 there came a marked change for the worse. Roentgenograms of the chest taken on November 5 showed generalized clouding of the right pulmonary field, with opacity in the base of the right lung and some fluid in the left pleural cavity. The roentgenologist's opinion was that this was due to malignant involvement of the mediastinum and hilus.

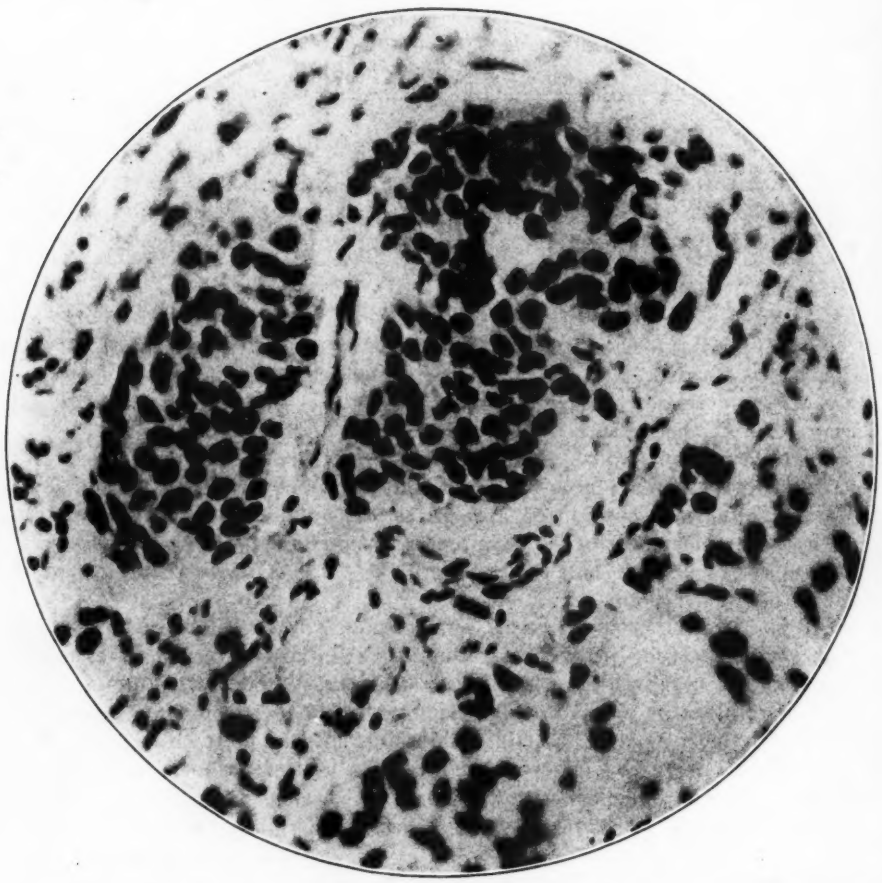

Fig. 1.—Photomicrograph showing carcinoma of the breast (surgical specimen).

On Jan. 20, 1935, after a fall, the patient was found to have a fracture of the neck of the left humerus, with little displacement. A roentgenogram did not reveal any evidence of metastasis of carcinoma in this region.

Death occurred on March 21.

Ocular History.—On Jan. 14, 1930, the patient was seen by one of us (A. N. L.), because of the complaint of diminished vision. This was due to incipient cataracts. Corrected vision at this time was 20/20 in each eye.

On Dec. 9, 1933, vision in the right eye was 20/50—2; after correction it was 20/20. Vision in the left eye was 20/200; after correction it was 20/30+. The left lens was diffusely hazy, with rather marked radiating cortical opacities below, which extended nearly to the center of the lens. The right lens was about the same as at the preceding examination.

On Jan. 23, 1934, vision in the right eye was 20/30—2 with correction; that in the left eye was 8/200 and was not improved by lenses.

Ophthalmoscopic examination of the left eye revealed a retinal detachment in the lower half. Metastasis to the choroid was suspected at that time. The tension was 21 in the right eye and 16 in the left (Schiötz). The field of vision of the right eye was normal; that of the left eye was limited to the lower half. The detachment became progressively worse, and vision decreased to nil.

On May 18 the patient had complained of diminution of vision in the right eye of several days' duration. Examination of the fundus revealed edema of the retina, extending temporally from the disk to the equator. Seven hemorrhages were noted around the macular region and near the disk. These hemorrhages as seen through the edematous retina appeared to be in the deeper layers of the retina. This was probably the time that the carcinomatous embolus lodged in a vessel in the choroid, but on account of the edema it was impossible to see the definite location of this metastatic growth. On July 25 the hemorrhages in the right eye had been absorbed, and the edema had subsided. Transillumination showed normal reflexes in both eyes. The cataracts seemed to be progressing more rapidly.

TABLE 3.—*Roentgen Treatment of the Left Eye*

Date	Site of Treatment
9/17/34	Anterior part through lids
9/21/34	From the temporal side
10/ 8/34	Anterior part
10/10/34	Temporal side
10/17/34	Anterior part
10/22/34	Temporal side
10/24/34	Anterior part

On August 4 the patient began to complain of pain in the left eye, so severe as to be accompanied by nausea and vomiting. The conjunctiva was markedly congested, the cornea hazy and the pupil widely dilated. The tension was 4 plus (determined by palpation). Transillumination showed a suspiciously cloudy area far back in the lower temporal quadrant. The patient was given physostigmine and pilocarpine, to be instilled into the left eye every three hours. The tension at first decreased and then increased and on August 20 registered 60 (Schiötz). The pain had become more severe, requiring opiates for relief. The cloudy area seen on transillumination had enlarged. On August 28 the left eye was enucleated. The patient made an uneventful recovery.

On September 12 the patient was still able to read moderately large print and attend to her correspondence with the right eye.

On September 16 the retina of the right eye was hazy, and a detachment was noted in the lower quadrant; the retina was elevated 15 D. Vision was limited to movements of the hand at 3 feet (91.4 cm.).

On September 17 roentgen treatments were begun by Dr. McDermott and Dr. Virden and continued as shown in table 3. The dose was 235 roentgen units at 140 kilovolts and 4 milliamperes, applied at a distance of 20 inches (50.8 cm.) through a filter of 0.25 mm. of copper and 3 mm. of aluminum.

On September 28 the detachment involved the lower half of the retina to the limit of the ophthalmoscopic field. The maximum elevation of the retina was 16 D., but vision had improved to counting fingers at 10 feet (3 meters). The visual field, with a 5 mm. object, was slightly contracted below and limited to 10 degrees above. Transillumination revealed an indefinite shadow far back and extending downward and outward. The retina was edematous and rather pale, and the macular area was irregularly mottled, but there were none of the yellowish areas mentioned by other writers.

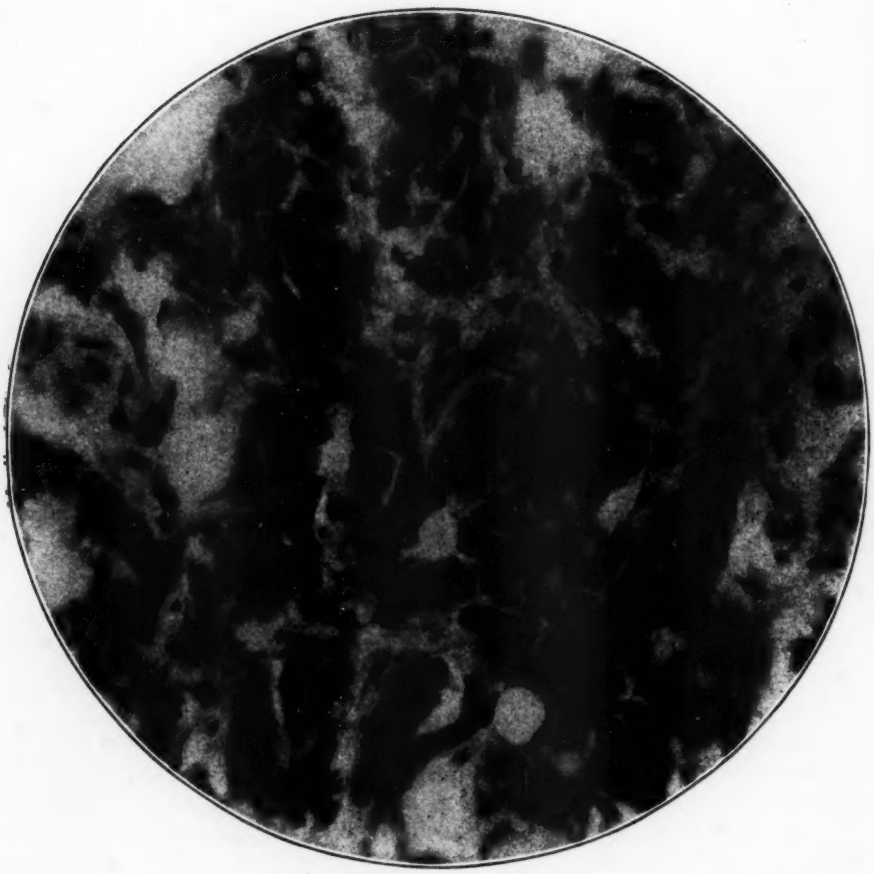

Fig. 2.—Photomicrograph taken post mortem, showing metastatic carcinoma of the lung.

On October 15 definite improvement was evident. The peak of the elevation of the lower part of the retina was only 8 D. Gradual improvement, both subjective and objective, continued under radiation therapy.

On December 19 there appeared to be about 1 D. of elevation of the lower part of the retina, with rather marked pigmentary changes about the macula and along the lower temporal artery. The lens apparently had not changed much as the result of radiation therapy. The patient was able to read and write. Vision in the right eye was 15/50 with correction.

On March 16, 1935, there were pigmentary changes involving the lower half of the fundus, extending to slightly above the macula and to the extreme nasal and temporal portions. This area corresponded to the area of the former detachment and had the characteristic appearance of a reattached retina. The pigmentary changes were most marked in the macular region and along the inferior temporal artery. Vision in the right eye was 20/50 + with correction. The peripheral field showed slight concentric contraction but no defects corresponding to the pigmentary changes. The patient was able to recognize all the colors with the 1 degree target. From this time there was little change in the eye until shortly before death, when the patient again complained of diminution of vision. Through the undilated pupil the retina did not seem to be elevated, but pigmentary changes had advanced. At no time was there any increase of tension.

Autopsy (Dr. E. T. Johnson).—Gross Appearance of the Lungs: A few small nodules measuring up to 1.5 cm. in diameter were observed in both lungs; one nodule, 3 cm. in diameter, was present in the right side of the mediastinum. No malignant process was observed in the gastro-intestinal or the genito-urinary tract or in the liver. The subcutaneous nodules appeared to be carcinomatous.

Microscopic Appearance of the Lungs (fig. 2): The lungs showed areas of pneumonitis with hemorrhage and necrosis, and, surprisingly, many of these areas showed few or no carcinomatous cells. Other areas, however, showed well defined secondary carcinomatous invasion of the lungs, which was most marked in the peribronchial lymphatics. The carcinoma cells were fairly uniform in size, shape and staining characteristics and were definitely malignant. Subcutaneous nodules from the region of the scar resulting from the amputation showed typical cellular architecture of carcinoma simplex. The remainder of the report on the autopsy is of no significance with respect to this study, with the exception of the report on the eyes, which will be discussed separately.

Pathologic Examination of the Eyes.—Gross Appearance of the Left Eye (Antemortem Specimen) (fig. 3): We found the globe to be of normal size and shape and firmer than normal. Sagittal hemisection revealed a complete retinal detachment, the separated retina appearing as a funnel-shaped central mass. The consistency of the subretinal exudate was that of very tough gelatin, much firmer than the usual consistency of such exudates. A flat mass was visible just within the sclera, entirely surrounding the optic nerve, extending forward about half-way to the equator. The maximum thickness was 1.2 mm.

Microscopic Appearance of the Left Eye (fig. 4): The cornea was thickened; the fibers were edematous, and there was more separation of the lamellae than would be expected in a globe fixed immediately after removal. The epithelium was intact (except for a small area of denudation), with slight vacuolation of its inner layers. The endothelium was markedly vacuolated and degenerated. The stroma of the iris showed evidence of senile atrophy with ectropion uveae. The pigment epithelium appeared normal. The filtration angle was almost obliterated, and there were some beginning peripheral synechiae.

The ciliary body was detached except at its anterior extremity. This was probably an artefact. The muscle fibers were apparently normal for the patient's age. The stroma of the ciliary processes showed early hyalinization. The ciliary epithelium contained rather sparse pigment granules, and the cells were somewhat swollen.

The lens did not appear in this section.

The detached retina was degenerated, the layer of rods and cones showing, as would be expected, the most marked change. Nuclei in the other layers were only slightly degenerated, but the cytoplasm showed more marked change.

At the posterior pole, on both sides of the entrance of the optic nerve, between the sclera and the choroid and infiltrating both layers, the choroid more than the sclera, appeared a flat tumor composed of nests of cells embedded in a fibrous stroma. In some places these cell nests assumed a pseudo-acinar architecture. They were identical with those seen in the tumor of the breast and those observed post mortem in the lungs and in the subcutaneous nodules in the region of the amputated breast and appeared definitely malignant, although they were probably of low grade malignancy. Only a few nuclei suggested mitosis. The cytoplasm appeared somewhat degenerated in places, but most of the nuclei stained well. Scattered pigment cells appeared throughout the tumor. An occasional cell nest

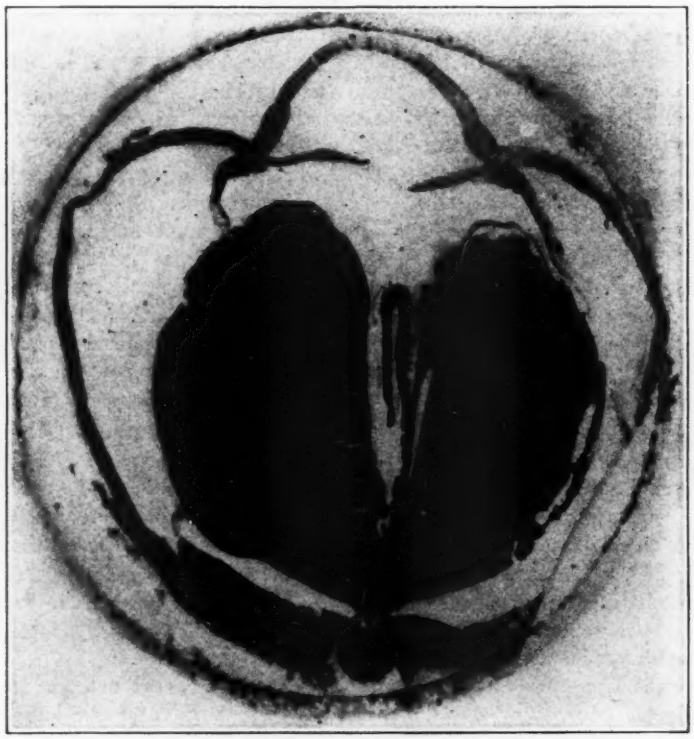

Fig. 3.—Section of the left eye, showing a thick tumor at the posterior pole, detachment of the retina and coagulated subretinal exudate (surgical specimen).

showed degeneration of the nuclei and cytoplasm of the inner cells, the outer cells having the normal staining characteristics of cancer cells. In the lower half of the section, near the nerve there were five small areas in which no tissue architecture could be made out, the space being filled with a loosely trabeculated, partly degenerated fibrous tissue, in which were embedded plasma cells and occasional leukocytes and pigment cells. The tumor cells at the margins of these spaces did not show more degeneration than elsewhere. It is probable that these spaces represented areas of degeneration of the choroid by pressure from the tumor without invasion. There was an area of fibrosis without tumor cells above the disk. This area was as thick as the adjoining areas of tumor and probably represented a relatively large area of tumor stroma.

Over most of the tumor the inner layers of the choroid were present, although degenerated and hyalinized. The relationship between the outer layers of the choroid and the inner layers of the sclera was distorted, and tumor cells were seen invading the sclera here and there.

The choroid was essentially normal in areas where it was not invaded by the tumor. In the posterior portions the pigment epithelium of the retina was adherent to the subretinal exudate and detached from the choroid. Its inner surface was rather more irregular than normal, this irregularity being due to heaping up of pigment cells. Within the subretinal exudate, in contact with the pigment

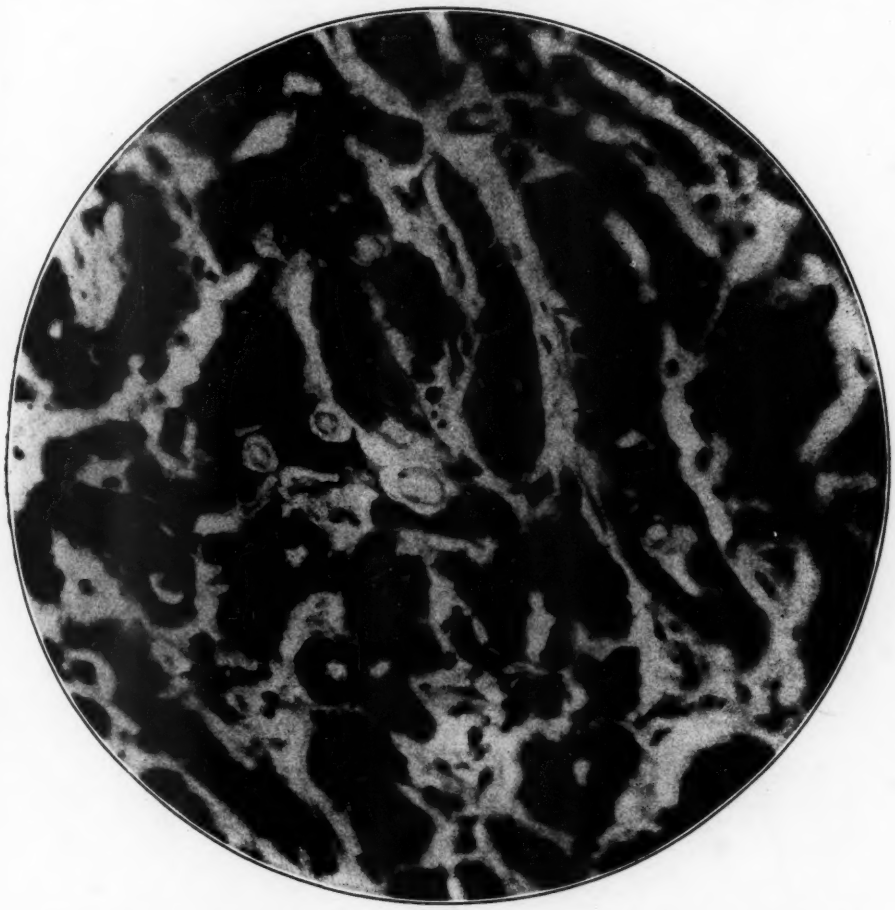

Fig. 4.—Section of the left eye, showing tumor cells; high power magnification. Compare the appearance of the individual cells with that of the cells shown in figure 9.

epithelium and in places in contact with the outer surface of the detached retina, were irregular clumps of cells with pale cytoplasm and rounded, oval or slightly irregular nuclei.

These cells were about the size of cells of the pigment epithelium, and the intensity of their nuclear staining was about the same. Many of them contained pigment granules. They probably represented proliferating pigment epithelium.

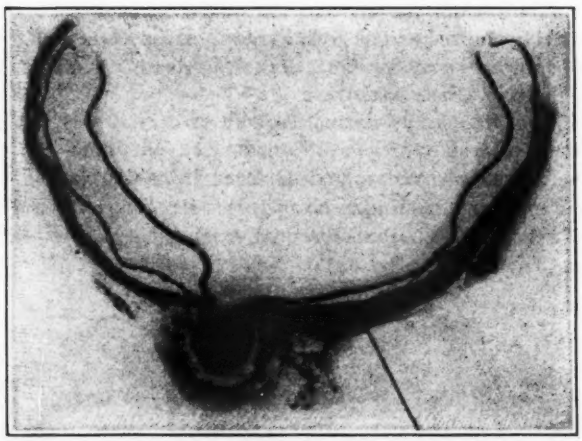

Fig. 5.—Posterior pole of the right eye (postmortem specimen). The arrow shows the location of the tumor.

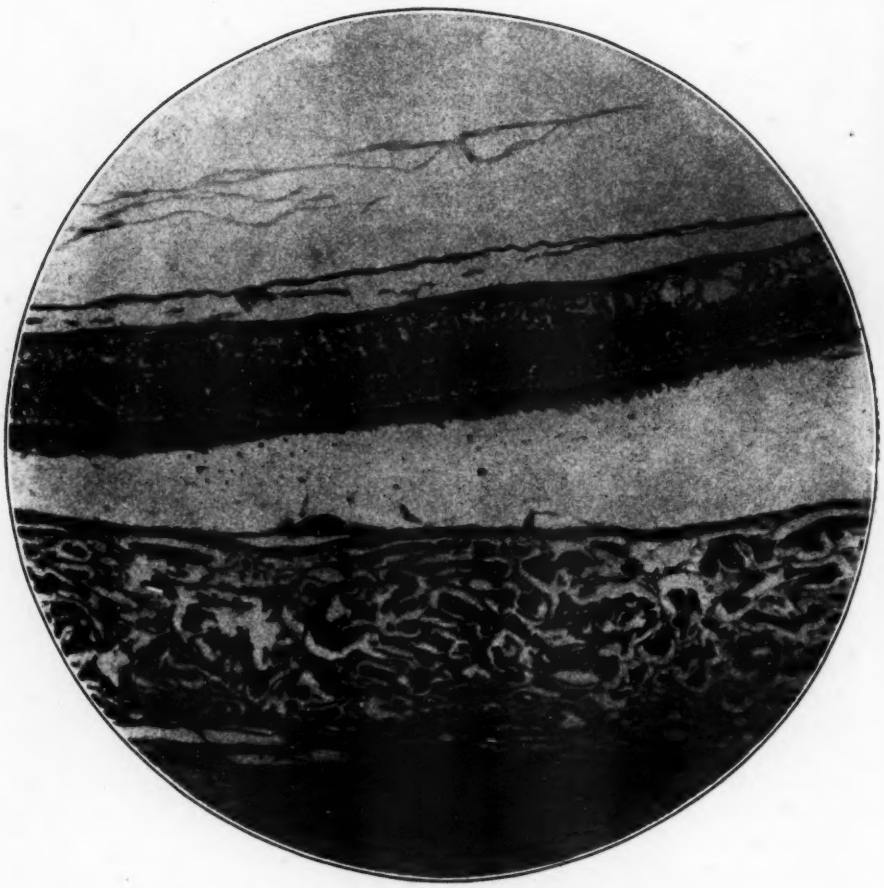

Fig. 6.—Section of the right eye, showing the general appearance of the tumor. There is irregularity of pigment epithelium in the area of retinal detachment.

The optic nerve presented no pathologic changes.

Gross Appearance of the Right Eye (Postmortem Specimen) (fig. 5): There was a moderate amount of postmortem change, and all discussion will take this change into consideration. The globe was of normal size and shape. Hemisection revealed no gross deviation from the normal. The retina was not detached in any place.

Microscopic Appearance of the Right Eye: Considering the postmortem changes, the anterior segment was essentially normal. The epithelial structures showed more degenerative changes than in the left eye. This was to be expected, since the specimen was not obtained until several hours after death.

Fig. 7.—Section of the right eye. Compare with figure 4.

The corneal stroma was more nearly normal and the endothelium less degenerated than in the left eye. The stroma of the iris was perhaps more atrophic and the pigment layers slightly darker than in the left eye. The ciliary muscle and processes were essentially similar to those in the left eye, except that the ciliary epithelium showed more pigmentation.

The retina (fig. 6) was detached throughout the section, but since in one area the pigment epithelium was separated from the choroid and in contact with the

retina this detachment was probably an artefact. This was borne out by the absence of subretinal exudate. The retina showed considerable postmortem degeneration, especially in the layers of rods and cones and their nuclei. The cytoplasm in the nuclear layers was degenerated, but the nuclei stained well. The fiber layers were degenerated, although the nuclei of the ganglion cells appeared nearly normal. The rods and cones were more degenerated over the tumor.

On the temporal side of the nerve (fig. 7), extending forward to the equator, was a tumor in which the clumps of cells presented approximately the same appear-

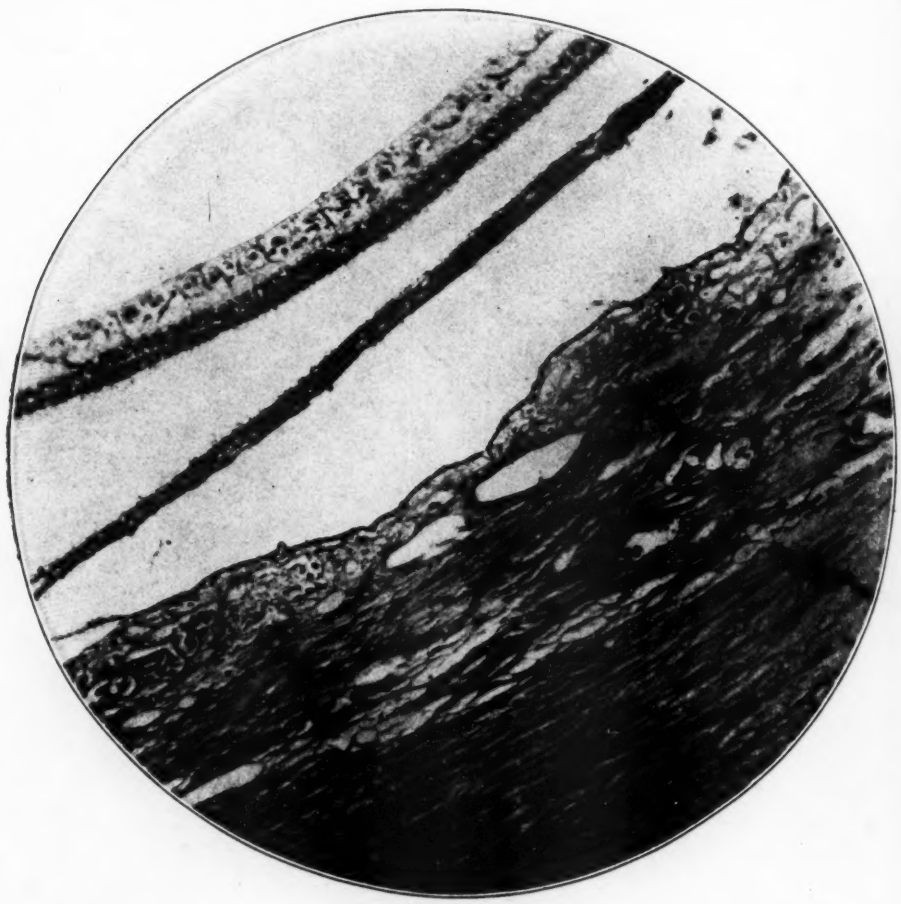

Fig. 8.—Section of the right eye, showing the scarred area in the tumor.

ance as in the right eye. Under high power magnification, however, it was evident that the majority of the nuclei of the tumor cells were necrotic, as evidenced by their much lighter staining and the irregularity of chromatin. There were proportionately about as many normal cells in this section as necrotic cells in the section from the left eye. The cytoplasm also appeared very ragged. Mitotic figures seemed to be absent.

Next to the nerve there was an area showing mostly degenerating tumor cells, embedded in a fibrous stroma which was more dense than that in the left eye.

Anterior to this was a fibrotic area (fig. 8) at least three times the normal thickness of the choroid, in which there were only a few cords of cancer cells that had retained fairly normal staining characteristics. Anterior to this the choroid assumed a more normal structure, although much thickened and containing a few clumps of cells; still farther anteriorly the choroid was practically normal. This fibrotic area was much larger and denser than that referred to in the right eye, and gave the impression of scarring rather than simply replacement of normal tissue. Under low power magnification the maximum thickness of the tumor was approximately 0.4 mm.

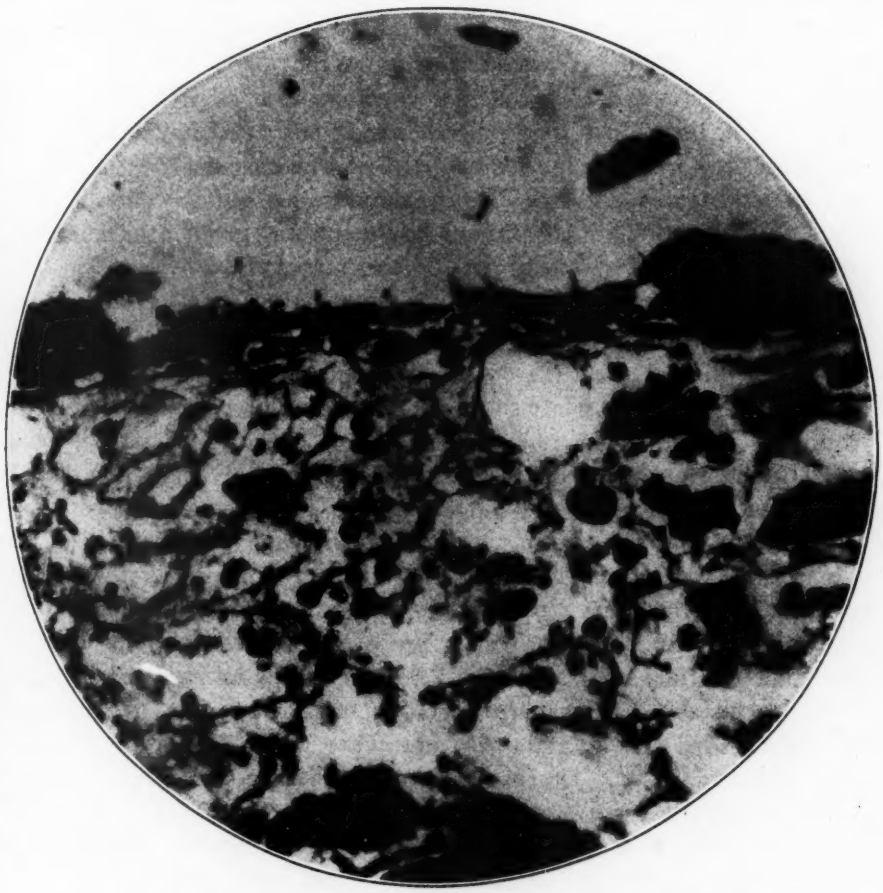

Fig. 9.—Section of the right eye, showing pigment epithelium and irregularity in the area of detachment of the retina; high power magnification.

On the nasal side of the disk there are no cancer cells, and the choroid appeared essentially normal.

The pigment epithelium appeared normal on the nasal side of the section. On the temporal side (fig. 9), overlying the tumor, there was a marked irregularity of distribution of pigment, some areas being almost completely depigmented, while elsewhere the pigment was heaped up in clumps. This corresponded to the pigment mottling seen ophthalmoscopically after reattachment of the retina.

COMMENT

So far as we have been able to find, ours is the first case reported in which treatment of a metastatic carcinoma of the choroid was successful and in which the diagnosis was proved at autopsy. Uckermann [11] reported a case of *cancer en cuirasse* in a woman aged 35 in whom both fundi "showed from the center to the periphery, grayish white, somewhat pigmented warts," with a detachment of the retina in both eyes. A clinical diagnosis of metastatic carcinoma was made, and three roentgen treatments were given over the eyes during a period of four weeks. In the right eye vision improved from 5/50 to 5/10, and in the left eye, from counting fingers at 3 meters to 5/50. The report was made during the patient's lifetime; hence no microscopic diagnosis was possible. Zentmayer [12] reported the case of a woman aged 60 in whose eyes were observed flat yellowish gray infiltrations of the choroid, elevated from 5 to 7 D. One radium treatment was given over the eyes, and roentgen radiation was applied to the site of the amputated breast. No report was made regarding vision either before or after treatment.

In our case we were able to observe the progress of the metastatic tumor in both eyes from the onset. It is possible that the actual cancer embolus had entered the left choroid a short time previous to our examination of Dec. 9, 1933, and because of the opacities of the lens the initial lesion was not seen, the first lesion observed being the retinal detachment noted six weeks later. In the right eye metastasis was suspected on observation of a retinal hemorrhage on May 18, 1934, although the detachment did not occur until four months later. Roentgen treatment then was successful in restoring useful vision until the final stages of life. In considering the pathologic observations, one is immediately struck by the marked difference in the microscopic pictures of the metastatic tumors in the two eyes. The marked fibrosis and cellular necrosis in the right eye are what might be expected from successful irradiation. The fibrotic area in the section of the left eye appeared more like the stroma of a scirrhous type of carcinoma than the dense fibrosis of scarring. Then, too, the extreme difference in thickness of the tumors, despite the fact that they were of approximately the same age, is further evidence of the successful result of treatment.

The proliferation and apparent migration of pigment in the pigment epithelium of the right eye explains the ophthalmoscopic observations after the reattachment of the detached retina.

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11. Uckermann, A.: Acta ophth. **6**:170, 1928.

12. Zentmayer, W.: A Case of Bilateral Metastatic Carcinoma of the Choroid, Arch. Ophth. **8**:616 (Oct.) 1932.

This is an encouraging result. There is no doubt that the low malignancy of the tumor greatly favored the successful outcome, but it would seem that in cases in which the metastasis is observed in its incipiency and the patient is not already moribund localized roentgen treatment offers hope of preserving vision.

Incidentally, in this case the period between the discovery of the primary tumor and the metastasis and that between the metastasis and death are among the longest recorded—forty-six months and fourteen months, respectively.

SUMMARY

The literature on metastatic carcinoma of the choroid and uveal tract is reviewed and brought up to date.

A case of bilateral choroidal metastasis of carcinoma of the breast is reported in which both metastastic tumors were observed almost from the time of the initial lodgment of the emboli.

Roentgen therapy was successful in restoring useful vision in the second eye.

The clinical diagnosis was confirmed by microscopic study of both eyes.

906 Grand Avenue.

A METHOD FOR THE CORRECTION OF ENTROPION IN TRACHOMATOUS PATIENTS

WITH PARTICULAR ATTENTION TO THE ESTHETIC RESULTS

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For several years I have paid particular attention to the complications of trachoma, a disease that, according to statistics compiled by me, causes about 14 per cent of the ocular disorders in Brazil.

Besides studying the problems of a more or less theoretical value relating to this disease, I have paid attention to its therapy. As a result of my studies in this field I can now state that, with an opportune combination of remedies in association with technical methods which will be discussed in more detail in following articles, I have succeeded in obtaining the clinical cure of trachoma in all my patients.

I use the term clinical cure because I am under the impression that the disease, at least in some cases, remains in a latent stage, even though a careful objective examination and a study of tissue removed for biopsy prove that the process is perfectly cicatrized.[1] And, besides, the presence of a latent micro-organism, under the light of the present knowledge of pathology, would not be surprising.

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1. Owing to the fact that I have observed a flare-up of the trachomatous process in two cases of traumatic ulcer due to a foreign body, I am led to believe that in cases of trachoma in which the condition was clinically cured the infection may remain latent. In one case this took place eight months after the patient had left my clinic. In the other case the flare-up occurred twenty-six months after the patient had left the clinic. In this period of time neither patient had a recurrence. The recurrence was limited to the traumatized eye. It was severe in the second patient, who had come the first time with trachoma in the second stage, with large nodules in the bulbar conjunctiva of both eyes and with pannus in the superior half of the cornea of the right eye and extending over the whole surface of the cornea of the left eye. The trauma caused a small ulceration in the internal quadrant of the cornea about 3 mm. from the limbus. The ulcer became infected, and in a few days characteristic trachomatous pannus developed, with involvement of the conjunctiva. A few parenchymatous blood vessels appeared in the cornea. In spite of the treatment complete pannus formed in the cornea six days following the trauma. Three months were required for cure. The patient has had no recurrence within the last three years. In the first case the recurrence was of less duration and less severe; healing was obtained in two months.

For more than five years I have followed several hundreds of patients who have been treated by this method, and I can say that recurrence is rare; if it does occur the condition is completely cured after a new brief course of treatment.

This method of therapy is based on the removal of the superior tarsal bundles of the orbicularis muscle, a procedure which I perform systematically on the trachomatous patients after the inflammatory process has stopped. I have decided to perform this systematic removal of the muscle because I have observed that in these patients the orbicularis muscle is, as a rule, hypertrophic, and it is my opinion that this hypertrophy is the principal cause of the entropion. The hypertrophic marginal fibers when contracted exert an abnormal pressure on the free margin of the tarsus and in this way cause the entropion. The muscular hypertrophy is a reflex action caused by the corneal lesions, which, as I had the opportunity to demonstrate in other articles,[2] are due to the primary localized infection of the cornea, caused by the continuity of the process from the superior part of the fornix to the limbus, and not to a secondary infection, which is held by many.

As I have already mentioned, the method that I use to obtain a diminution of palpebral pressure on the cornea consists in surgical procedures already in use which I have modified so as to assure myself of their success and to eliminate complications.

RÉSUMÉ OF PROCEDURE

Following is a résumé of the procedure:

1. Anesthesia is produced, and the skin is incised in a line parallel to the free border of the lid about 5 mm. above it. (fig. 1).

2. The skin is pulled inward by the thumb and freed to the height of the superior margin of the tarsus with small incisions; then at this level an incision of the muscle is made through its thickness down to the tarsal plate (fig. 2).

3. The distal side of the cutaneous flap is freed inferiorly down to the cilia, and a small zone of the tarsus is denuded close to them (fig. 3*b*).

4. All the muscular bundles between the superior and the inferior incisions of the muscle are removed with the scissors (fig. 4).

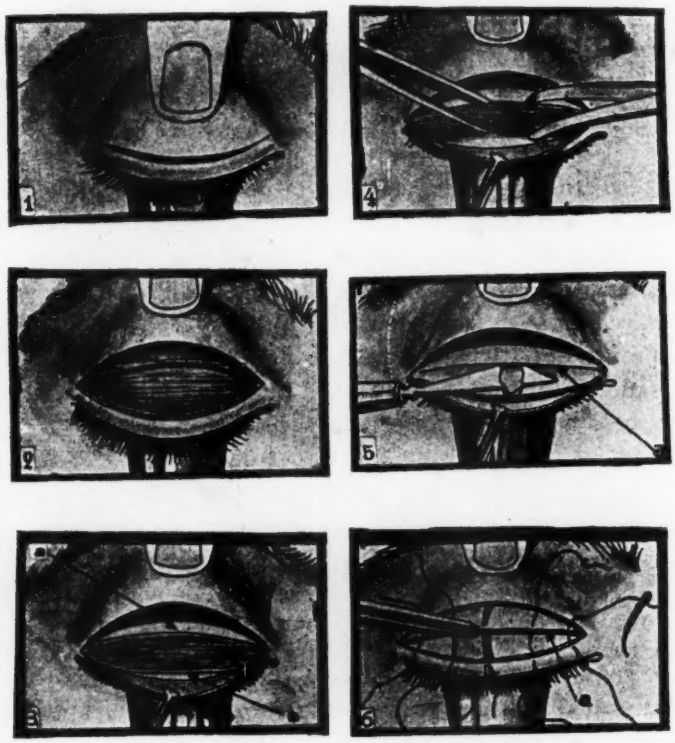
5. A linear incision is made on the tarsus about 5 to 8 mm. from and parallel to the free border of the lid, care being taken not to reach

2. Busacca, A.: Die trachomatöse avaskuläre Keratitis, Klin. Monatsbl. f. Augenh. **94**:202, 1935; Die Entfernung des Tarsalteiles des Orbikularmuskels des Oberlids zwecks Bekämpfung des Entropiums und der Trichiasis zur Verhinderung von Rückfällen des trachomatösen Prozesses, Ztschr. f. Augenh. **88**:100, 1936.

the conjunctiva (fig. 5*a*). Then thin slices of the tarsus are removed with the knife, from the cilia up to the tarsal incision (fig. 5), so that a small furrow-like incision will be formed in this region (fig. 6).

6. The inferior lip of the wound is sutured to the superior side of the tarsal flap, after it is assured that the suture will not pass between the cilia.

The purposes of this method are the following: (*a*) to remove completely the muscular bundles pressed between the skin and the tarsus



Figs. 1 to 6.—Steps in operation for entropion complicating trachoma.

and (*b*) to remove portions of the thickened tarsus due to the trachomatous process so as to restore to the lid a structure which is similar to the normal and to bring back the cilia to their natural position.

COMMENT

In order to gain the best results obtainable by this procedure, especially from the esthetic point of view, one must not overlook a few details that one can appreciate only after having used this procedure on several occasions and after having noticed imperfect results due to an incorrect technic.

I should like to dwell on these points:

How Far from the Margin of the Lid Should the Incision of the Skin Be Made?—The condition of the lids must guide one in the choice of distance, because these have a great influence on the future position of the normal fold of the superior lid, which in the trachomatous patient is often flattened out. The lids will remain in the correct position because of the large surface of adhesion between the tarsus and the skin, especially after the suppression of the action of the orbicularis muscle. Incision too close to the free margin will not give the necessary furrow (or sinking in), and if the skin of the lid is too abundant this may give the impression of pseudoblepharochalasis. If the incision is made too far from the margin, because of its vast adhering surface the fold will sink so as to produce a poor cosmetic effect.

At What Distance Should the Tarsal Incision Be Made?—If the incision in the skin has been made correctly it is convenient to let the

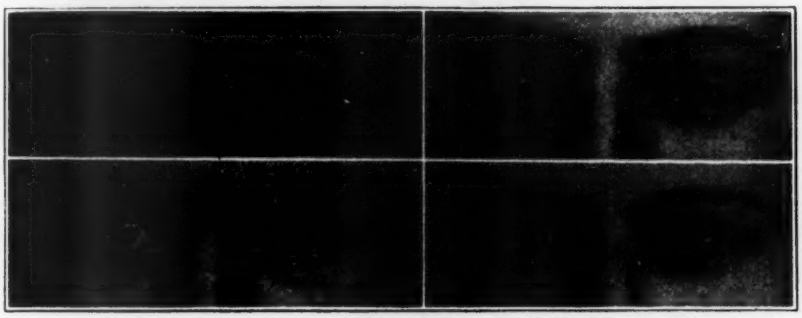


Fig. 7.—*A*, appearance of patient just before the operation on the left eye; the right eye was operated on three weeks before. *B*, appearance of patient one year after the operation on the left eye. *C*, appearance of patient previous to the operation on the left eye; the right eye was operated on four weeks before. *D*, appearance of patient four months after the operation on the left eye.

size of the inferior cutaneous flap guide one. Usually I hold the middle portion of the inferior lip of the skin and with the forceps against the tarsus pull up the skin as much as possible so as to obtain a correct position for the cilia. The incision is made about 1 mm. above this point, but sometimes, because of special conditions of the tarsus, the incision cannot be made at this height. In such circumstances it is convenient to level the tarsus, avoiding injury to the insertion of the elevator, and then let the silk suture pass at the level of the superior border of the tarsus or through its fascia to give the cilia a correct position.

Thinning of the Tarsus.—One must pay particular attention to this process. The knife is directed perpendicularly against the tarsus imme-

diately behind the line of the cilia; then the knife is inclined about 90 degrees, and its edge is directed toward the line of incision already made on the tarsus. Only in this way can one remove thickened portions of the tarsus near the margin of the lid. It is understood that one must avoid injuring the roots of the cilia, because this would cause partial madarosis.

In those cases in which the tarsus is much thickened and granular, even above the line of incision, it is convenient to thin it out, leaving a step about 1 mm. deep.

Suture.—In order to obtain the desired cicatricial effect one must suture the inferior lip of the wound to the tarsal flap; generally five sutures are sufficient. It is preferable to employ semicircular needles, because the ordinary needles may tear the tarsus. The knot must be taut enough to obtain a good position for the cilia. Sometimes one must leave the knots slightly loose, because if they are too tight they cause an unesthetic hypercorrection.

The superior lip of the flap is left alone, and it is in this place that one gets a fold of skin. The sutures are placed close to the inferior lip of the flap and not between the cilia; they are removed forty-eight hours later, and because of the large surface of adhesions between the skin and the tarsus there is no fear of complications. Instead there is an advantage, since the sutures, being far from the palpebral margin, do not suppurate, and one does not get the formation of necrotic zones of skin or scars which give to the margin a lobular appearance that one ordinarily notices when other methods are employed.

Bandaging.—Bandaging is very important, as it serves to keep a close contact between the tarsal surface and the surface of the skin in the first twenty-four hours; it also prevents the formation of blood clots between the two surfaces.

To insure such close contact I cover the rough surface of the tarsus with a coagulant in powder form before suturing, and in this way I prevent small secondary hemorrhages. After the operation I place the lid in its correct position and spread some salve on the wound so as to avoid adherence with the dressing; then I fill in the cavity between the ridge of the nose and the superciliary arch with wet cotton. On top of this I place a layer of dry cotton and bandage. With this procedure one notices no edema or hemorrhages the following day. One can then remove the bandage, and the patient is able to return to work. Slight edema on the following day is of no importance.

Indications for Intermarginal Incision.—In some methods an intermarginal incision is used to keep the cilia away from the cornea, but, as is generally known, they cause thickening of the margin, which is not esthetic. I have been able to observe that the removal of the

orbicularis muscle and the thinning of the tarsus are sufficient to give a perfect correction to the position of the cilia in almost every case. Only in rare cases in which a group of cilia are more deviated than others and therefore the traction on the skin is not enough to bring them in a normal position do I have to resort to the intermarginal incision, limiting it to that portion where the cilia are more deviated. No matter how well performed this procedure is I have always noticed a permanent deformation of the margin in this position.

Indications for the Canthoplasty.—The process of trachomatous tarsitis, which, as is well known, takes place in the tarsus, causes shrinkage of the latter. This produces a reduction not only in height but also in length. Because the tarsus is fixed at the two canthi, which are situated in a plane posterior to that at the apex of the cornea, the shrunk tarsus is tense between these points of incision and compresses the cornea.

In these cases the removal of the orbicularis muscle is not sufficient to diminish the normal pressure of the lid on the cornea. It is in these cases that, in order to be sure of the effect of therapy, I perform canthoplasty about one week after the removal of the muscle. I use the classic process: incision at the external canthus, severance of the insertion of the external palpebral ligament from its periosteum and application of three sutures uniting the conjunctiva and the skin. At this point I should like to recall that in cases in which the condition is particularly serious and in which the corneal lesions are more resistant than usual to ordinary treatment I perform canthoplasty, with good results.

With the precautions just described I think that this procedure gives better results than others, especially from the esthetic point of view (fig. 7). In fact, the cilia take the normal direction, and the superior lid, deprived of its hypertrophic muscular bundles and with its thinned-out tarsus, becomes much thinner than before; a normal fold forms on the skin of the superior lid. In the trachomatous patients this is ordinarily absent or flattened out. Since the scar is at the bottom of the fold, it is not evident. As a consequence of the traction applied on the superior lid to fix the skin on the tarsus the free palpebral margin is slightly lifted, and the rima palpebrarum is a little wider than before. This gives a good cosmetic effect, because in most cases it is sufficient to correct a slight ptosis that one often sees after cicatrization of the trachomatous process.

Another point which must be taken into consideration is the fact that the palpebral border is kept away from the cornea, and consequently one notices that there is a small space between the posterior surface of the lid and the cornea. On account of capillarity a small amount of liquid remains between them.

Other Possible Points of the Process. — The procedure just described, with a few variations, can help every time that one wishes to reconstruct the fold of skin in the superior lid. I have had the opportunity to use it twice, with very good results, as a complement to the Blaskovics operation for ptosis.

Even when a good correction of the ptosis is obtained one observes a difference between the normal eye and the eye that has been operated on, because in the latter the fold of skin is formed immediately close to the margin, which gives an appearance of a double lid. In such cases after the cutaneous incision has been made and the lips of the wound spread apart, a muscular incision is made at the level of the superior border down to the tarsus. Then by spreading the fibers of the orbicularis muscle, but without removing them, the skin of the inferior lip of the incision is sutured to the superior border of the tarsus, leaving the superior lip free. In my experience, the fold formed in its right position, and the esthetic effect was excellent.

ANOMALOUS OPHTHALMIC ARTERY WITH OCULAR SYMPTOMS

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Many cases of disease of the intracranial blood vessels have erroneously been reported as cases of orbital aneurysm or aneurysm of the ophthalmic artery, and several cases have been cited under these titles in the literature with no definite reports to verify the occurrence of the condition. Axenfeld in his textbook [1] merely mentioned the occurrence of "that extremely infrequent affection" circoid aneurysm of the ophthalmic artery. In de Schweinitz' textbook [2] it is stated that pulsating exophthalmos was formerly regarded as evidence of true aneurysm of the ophthalmic artery, an assumption probably based on the observation of Guthrie,[3] who early in the nineteenth century demonstrated at autopsy the presence of an ophthalmic aneurysm which had been associated with pulsating exophthalmos.

De Schweinitz and Holloway [4] in their well known brochure on pulsating exophthalmos summarized 44 cases of this disease which had been reported in the literature up to 1907 and found among this number 3 in which the condition was attributed to anomalies of the ophthalmic artery, though no definite reference regarding the report of these cases was given.

Casey Wood [5] also cited statistics, including those for 19 autopsies in cases of pulsating exophthalmos among which true aneurysm of the ophthalmic artery was said to have been present in 2 instances, without giving definite references as to the time and place of publication.

Charles Stedman Bull [6] mentioned 2 cases of endocranial aneurysm of the ophthalmic artery seen in the cadaver and 2 cases of orbital aneurysm, without giving a definite bibliography.

Read before the American Ophthalmological Society, Hot Springs, Va., June 1, 1936.

1. Axenfeld, Theodor: Lehrbuch der Augenheilkunde, ed. 6, Jena, Gustav Fischer, 1920, p. 91.

2. de Schweinitz, George: Diseases of the Eye, Philadelphia, W. B. Saunders Company, 1921, p. 641.

3. Guthrie, G. J.: Lectures on the Operative Surgery of the Eye, London, J. Butler, 1837.

4. de Schweinitz, George, and Holloway, Thomas: Pulsating Exophthalmos, Philadelphia, W. B. Saunders Company, 1908, p. 44.

5. Wood, Casey: American Encyclopedia and Dictionary of Ophthalmology, Chicago, Cleveland Press, 1915, vol. 7, p. 4861.

6. Bull, Charles Stedman, in Norris, W. F., and Oliver, C. A.: System of Diseases of the Eye, Philadelphia, J. B. Lippincott Company, 1898, p. 31.

Judging from the present knowledge of the frequency of aneurysms in general, the figures as to the relative frequency of anomalies of the ophthalmic artery would appear to lead to an overestimation of the occurrence of lesions of the ophthalmic artery. However, it is probable that the various indefinite citations all referred to identical publications. Analysis of those cases in which the condition was reported as aneurysm of the ophthalmic artery or as orbital aneurysm and in which clinical and postmortem study were included bears out this inference. A chronological review of the literature by Frost in 1883 [7] included 19 cases of pulsating exophthalmos in which the patient was subjected to autopsy. In 2 of these, an aneurysm of the ophthalmic artery—presumably idiopathic—was demonstrated, in the one by Guthrie [3] and in the other by de Villard,[8] and in 1 an aneurysm by anastomosis was demonstrated by Nunnelley.[9] In a later compilation by Rivington,[10] including reports of 12 cases, 1 instance of supposedly true aneurysm of the ophthalmic artery was cited (the case of Guthrie). Various tabulations by other authors included data on the same cases. The most comprehensive survey of the literature on intracranial aneurysm up to 1920 was published by Sattler.[11] In his analysis he regarded the case published as one of aneurysm of the ophthalmic artery by Travers [12] in 1809 as the first of its kind in the literature. A few years later Dalyrample [13] reported a similar case. However, in both these cases the condition definitely represented an aneurysm by anastomosis, and in both the aneurysm was cured by ligation of the common carotid artery.

The first authentic case which was generally accepted as one of a true aneurysm of the ophthalmic artery is that observed by Guthrie [3] in 1823. This was a case of bilateral pulsating exophthalmos in which necropsy revealed an aneurysm of the ophthalmic artery as large as a hazelnut in each orbit. Although no mention was made of the condition of the other cranial vessels, the history of pulsating exophthalmos in this case would lead to the inference that the aneurysm in this case was not of spontaneous origin but that it occurred as a complication of an anastomosis between the internal carotid artery and the cavernous sinus. However, Guthrie considered his case as one of true ophthalmic aneurysm and maintained that such lesions are the primary cause of pulsating

7. Frost, W. A.: Tr. Ophth. Soc. U. Kingdom **3**:9, 1883.

8. de Villard, Carron: Guide protique pour l'étude d. malais des yeaux, Dissert., 1838, p. 484.

9. Nunnelley: Med.-Chir. Tr., London **42**:165, 1859.

10. Rivington, W.: Lancet **1**:1559, 1896.

11. Sattler, C. H., in von Graefe, A., and Saemisch, E. T.: Handbuch der gesammten Augenheilkunde, Leipzig, Wilhelm Engelmann, 1920, vol. 1, pt. 2, p. 9.

12. Travers: Med.-Chir. Tr., London **40**:113, 1809.

13. Dalyrample: Med.-Chir. Tr., London **6**:111, 1819.

exophthalmos. His hypothesis influenced subsequent observers to designate many of their cases of pulsating exophthalmos as cases of ophthalmic or orbital aneurysms.

A case reported as one of spontaneous aneurysm of the ophthalmic artery by Nunnelley [9] revealed post mortem an aneurysm of the artery before its entrance into the optic canal, lying partly in the sella turcica and compressing the ophthalmic vein. There was a history in this case of pulsating exophthalmos of three weeks' duration five years previously, with relief of symptoms after ligature of the internal carotid artery; hence Sattler [11] in his appraisal of the case considered it to be not one of a true aneurysm but one of an aneurysm occurring coincidentally to an intracranial vascular lesion, presumably a communication between the endocranial portion of the ophthalmic artery and the ophthalmic vein.

Considerable doubt also exists regarding a case observed by de Villard [8] in which an aneurysm of the ophthalmic artery at the entrance of the vessel into the orbit was observed at autopsy. Whether or not the case could properly be classed as one of true aneurysm is problematic, as the patient was not seen during life and hence symptoms indicative of disease of the blood vessels had not been elicited.

Another doubtful case is that reported by Ritter,[14] in which an orbital aneurysm of the ophthalmic artery was demonstrated at postmortem study but in which there had been no clinical evidence of aneurysm during life. No mention was made of the condition of the larger intracranial vessels in either of these 2 cases to verify or disprove the diagnosis of spontaneous enlargement of the ophthalmic arteries.

The same doubt may be offered regarding the case of Zuckerkandl,[15] who reported observing at postmortem examination an aneurysm of each ophthalmic artery within the cranium in a boy blind from atrophy of both optic nerves but who made no reference to the condition of the larger basilar vessels to verify or disprove the spontaneous nature of the aneurysm.

Reports of a number of instances of pulsating exophthalmos have appeared in the literature in which spurious aneurysms of the ophthalmic artery were present—mostly intracranial—in which the association of the vessel with a lesion of the carotid artery was definitely established clinically or by autopsy. Dempsey [16] observed an unusual case of this kind in which postmortem study disclosed a large fusiform aneurysm of the internal carotid artery associated with an intracranial fusiform enlargement of the ophthalmic artery to four times its normal size and

14. Ritter: Jahresb. d. Gesellsch. f. Nat.- u. Heilk. **10**:6, 1887.
15. Zuckerkandl: Wien. med. Jahrb., 1876, p. 350.
16. Dempsey, Alexander D.: Brit. M. J. **2**:541, 1886.

a saccular aneurysm of the artery within the orbit as large as a mandarin orange.

Notwithstanding the fact that the occurrence of primary idiopathic aneurysm of the ophthalmic artery has never been verified in any of the reported cases, such lesions evidently do occur, though undoubtedly they are rare. Search of the literature has failed to reveal a single case of ophthalmic aneurysm in which association of the lesion with disturbance of the larger intracranial vessels could be definitely excluded at postmortem examination. This observation would appear rather convincing. However, recent surgical disclosure of pathologic changes of the ophthalmic artery in a patient with an apparently normal internal carotid artery definitely established the occurrence of an anomalous distention of this vessel. With the increasing frequency of the surgical study of intracranial vessels ophthalmologists may expect some interesting observations, which eventually will probably lead to the demonstration of true aneurysms of the ophthalmic artery.

Apparently the first contribution in this direction was recently made by Drs. H. S. Sanford, M. Craig and H. P. Wagener.[17]

> The patient was a woman of 54 years who since her eleventh year had noticed a peculiar transient visual disturbance at each menstrual period and a definite defect in vision for several months prior to her examination on Oct. 11, 1935. At that time vision of the right eye had been reduced to 2/40, and with the left eye she was able to count fingers in only a small area of the upper nasal field. Perimetry revealed inferior altitudinal anopsia in the right field, with a functioning area only in the upper nasal quadrant of the left.
>
> Ophthalmoscopic examination showed questionable edema of the upper nasal margin of the disk of the right eye and a flat, slightly pale disk of the left eye. A diagnosis of chiasmal lesion of unknown nature was made. Operation was performed by Dr. Craig on Oct. 12, 1935. Transfrontal craniotomy on the left and exposure of the chiasm by lifting the frontal lobe revealed enlargement and tortuosity of both ophthalmic arteries. On the basis of the assumption that the pulsating vessels were compressing the optic nerves against the bony walls of the optic canals, the upper margins of the foramina and the roofs of the canals were excised. The operation terminated in recovery. Twelve days later vision in the right eye had improved to 6/12, and the fields were practically normal in shape though still somewhat constricted.

This probably is the first case in which a diseased ophthalmic artery was exposed by craniotomy and surgical treatment applied at the point of the lesion. The condition was not present in any of the cases which were previously published.

It was a strange coincidence that even before the report of the case observed by Sanford, Craig and Wagener had reached me I should have observed a case almost its counterpart.

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17. Sanford, H. S.; Craig, W. M., and Wagener, H. P.: Proc. Staff Meet., Mayo Clin. **10**:721 (Nov. 13) 1935.

REPORT OF A CASE

A white girl, aged 9, was referred for examination on Jan. 10, 1936, by Dr. Louis Casper, of Louisville.

History.—The mother stated that the first evidence of trouble appeared in August 1935, when it was noticed that the left eye sometimes crossed and that it was more prominent than the right eye. These symptoms gradually grew more pronounced, and after a time failure of the left eye to turn upward in accord with the other eye was noted. In making the endeavor to look upward the child complained of seeing double. A defect in vision of the affected eye had also been

Fig. 1.—Appearance of patient before operation, showing inability of left eye to rotate upward.

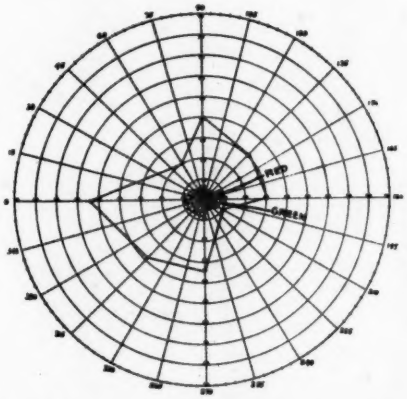

Fig. 2.—Left visual field before operation.

apparent for several months. The patient had not been aware of any other sypmtoms, such as pain or vertigo. Since the ocular symptoms were first noticed the patient had been under the care of an oculist, who had administered tuberculin three times a week for four months, with no improvement in the condition.

There was no previous history of injury or of any serious illness, other than scarlet fever and diphtheria in the patient's preschool years. There had been no previous ocular trouble, but the patient had worn glasses for several years to improve her vision.

The family history was not significant.

General Examination.—This showed a girl of average size, apparently well developed mentally and physically. General physical examination revealed nothing

abnormal. The Wassermann reaction of the blood was negative; the tuberculin test (Mantoux) gave negative results; roentgenograms showed no abnormality.

Ocular Examination.—This revealed deviation of the left eye downward and outward, with some proptosis. Measurement with the exophthalmometer showed 20 degrees of exophthalmos in the right eye and 25 degrees in the left. Sursumduction was limited, extreme effort barely bringing the eye to the midline. The pupils were equal in size and reacted normally to light and in accommodation. The sclera showed no evidence of an inflammatory reaction. The lenses and media were clear. The optic disk of the left eye was raised (between 3 and 4 diopters); the veins were distended and tortuous; the retina was slightly blurred in proximity to the disk. No retinal hemorrhages or effusions were visible. The right fundus was normal. Vision in the right eye with high degree cylinders was 20/20, and in the left, 20/70—3. The visual field of the right eye was wide and regular; that of the left was narrow (from 30 to 40 degrees), with constriction above and slightly outward to 10 degrees and below and slightly nasally to 20 degrees. The fields for red and green were very narrow. The blindspot was normal. No central scotoma was present.

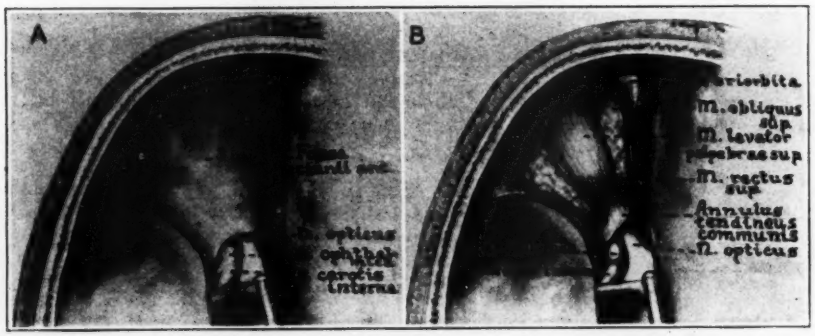

Fig. 3.—*A*, enlarged artery before removal of roof of the optic canal. *B*, orbital contents exposed by removal of the orbital roof.

Provisional Diagnosis.—The disorder was thought to be a lesion near the optic foramen. The nature of the lesion was problematic, although it was most likely neoplastic. A neurologic examination was advised, and it was thought that an exploratory operation might be necessary. The case was referred to Dr. Glen Spurling, to whom I am indebted for the report of the operation.

Operation.—On Jan. 20, 1936, operation was performed by Dr. Spurling, consisting of a frontal bone flap on the left and decompression of the left orbit, with the patient under anesthesia with tri-bromethanol in amylene hydrate and ether. An anomaly of the ophthalmic artery was found. The details of the operation are as follows:

A left frontal flap was turned down in the usual manner, with the incision completely concealed in the hair line. The dura was tense, and the ventricle was tapped in order to relieve the tension. The ventricle was apparently normal in size, and the fluid was clear. The frontal lobe, which was covered by dura, was reflected from the floor of the anterior fossa. The roof of the orbit, which consisted of dense bone, was removed piecemeal with rongeurs. All the bone was removed widely from the roof of the orbit down to and including the bone over the optic foramen. Then the dura was opened in line with the superior limb of

the bone flap in order that the optic nerve and the foramen might be directly inspected. Beneath the nerve and just lateral to it lay a large vessel, probably the ophthalmic artery. This was half again as large as the optic nerve and appeared to be running through the foramen beneath the nerve. The nerve appeared to be compressed.

Next, the capsule of the orbit was incised, and orbital fat with a large superior rectus muscle herniated into the opening. Carefully, bit by bit, the entire roof of the optic foramen was removed and the dura reflected from the surface of the optic nerve. The dura was incised the whole length of the optic nerve, thus affording adequate decompression of the nerve. There was no evidence of a tumor within the orbit. The superior rectus muscle, however, was unusually large, and in view of the vascular anomaly I felt that it would be unwise to resect part of the muscle at this time. After all the bleeding was carefully controlled the bone flap was replaced and sutured in layers with interrupted black silk sutures. The patient stood the operation well.

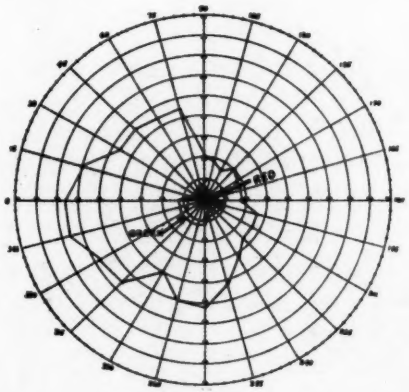

Fig. 4.—Left visual field four months after operation.

Course.—Two weeks after the operation slight hypotropia with some lateral deviation was still present, but the eye could be rotated somewhat above the horizontal meridian. Proptosis was less marked; papilledema was subsiding (2 diopters), and pallor of the optic nerve was apparent on the temporal side. Vision was 20/50 + 2.

When the child was last examined, on May 7, she was much improved. The blood vessels at the disk of the affected eye had returned to normal size, and the retina was of normal appearance. However, marked atrophy of the nerve had developed. The eye was still directed outward and downward, though not to the degree present when the patient was first examined. Rotation upward was not as limited as it was prior to the operation. Proptosis was hardly noticeable; the exophthalmometer reading was 20 degrees for the right eye and 22 degrees for the left. Vision in the left eye was 20/40 — 2. The field for form was wider but still limited above; the fields for color were still narrow. The failure of visual acuity, both central and peripheral, to return to normal in this case must be attributed to the probable prevalence of papilledema over a period of four or five months and the resulting atrophy of the optic nerve. Further spontaneous improvement in the hypotropia cannot be hoped for, owing to the destruction of the attachment of the superior rectus muscle brought about by the removal of the roof of the orbit.

COMMENT

Whether the distended artery observed in this case could strictly be placed in the category of a vessel with aneurysm is obviously problematic, as macroscopic distinction between an anomalous artery and an aneurysmal vessel is not possible. However, even in the absence of microscopic study of the walls of the vessel, it seems justifiable to look on an artery which has attained from two to three times its usual proportions as a potential aneurysmal vessel, even though a definite fusiform or sacculor state of distention has not been reached.

According to the figures of Locke,[18] spontaneous aneurysm usually occurs near the end of the fifth decade of life, though it has been observed in persons of all ages, including very young children, and it may perhaps be a fair assumption that many of the aneurysms observed later in life had existed for years and had become manifest only with an increase in size coincident with advanced age and structural changes in the arterial walls. Hence the age of our patient—9 years—could not be regarded as contradictory to the presence of a distended artery.

Statistics show definitely that arterial enlargements take place with greatest frequency within the cranium, a fact attributed to the relative thinness of the walls of the intracranial vessels. In a summary of 154 cases of aneurysm of the basilar arteries tabulated by Gowers [19] it was shown that the middle cerebral artery was involved 44 times, the internal carotid artery 23 times and the other vessels with relatively less frequency.

Several years ago it was my privilege to read a paper before the American Ophthalmological Society dealing with the part played by intracranial aneurysms of the arteries of the circle of Willis in the production of ocular palsies.[20] Attention was called to an analysis of 5,432 autopsies by Fearnsides [21] in which the presence of fusiform aneurysms of the basilar arteries was demonstrated in 44 instances. In most of them the etiologic relation between the lesions of the blood vessels and the motor disturbance was based entirely on conjecture. However, in recent years, since the cranial cavity has so frequently been explored in the living subject, such a relation has been definitely established. More recent clinical observations by Albright,[22] Symonds [23] and others indicate that in a certain number of cases aneurysms of the basilar arteries which are accompanied with intermittent apoplectiform seizures

18. Locke, C. E.: Ann. Surg., July 1914.
19. Gowers: Diseases of the Nervous System, Philadelphia, P. Blakiston's Son & Co., 1893, p. 259.
20. Pfingst, A. O., and Spurling, R. G.: Tr. Am. Ophth. Soc. **27**:227, 1929.
21. Fearnsides, E. G.: Brain **39**:224, 1916.
22. Albright, Fuller: Bull. Johns Hopkins Hosp. **44**:215 (April) 1929.
23. Symonds, C. P.: Guy's Hosp. Rep. **73**:139, 1923.

can be diagnosed during life by a study of the motility of the eyes, as the muscular involvement in these cases is not infrequently brought about by direct pressure of the distended blood vessels on the oculomotor nerves in their course from their superficial origin at the base of the brain to their entrance into the orbit.

One may perhaps conclude that the tendency of the vessels to bring about ocular signs increases with their forward position at the base of the brain, where their proximity to the third, fourth, fifth and sixth nerves made these nerves vulnerable. The fact has thus been rather well established that aneurysm of the internal carotid artery as such or when communicating with other vessels is the most frequent of the lesions of the cranial arteries to disturb the motor functions of the eye.

Ocular palsies occurring suddenly should at once lead one to suspect a lesion of an intracranial blood vessel, even in the absence of pain or other symptoms indicative of aneurysm, for it has been proved post mortem that an endocranial aneurysm may attain considerable size without exhibiting the clinical phenomena usually associated with this disorder. Beadles [24] has forcefully stressed the fact that the clinical triad characteristic of the spurious type of aneurysm seldom, if ever, occurs in a case of spontaneous intracranial aneurysm unless the artery ruptures or forms a communication with a sinus and thus pumps arterial blood into the venous circulation. He made the interesting observation that in 555 cases in which the presence of an arterial aneurysm was proved by necropsy murmurs were said to have been heard during life in but 2 instances and refuted the prevailing impression that pulsation with an isochronous audible bruit is the earliest and most common symptom of all forms of intracranial aneurysm. In the most recent survey of the literature on pulsating exophthalmos by Harkness [25] it was demonstrated that in the large majority of instances in which the lesion was spontaneous, 125 of which were reported by him, the condition was caused by a communication of the internal carotid artery with the cavernous sinus and that several of these cases were published under the title of aneurysm of the ophthalmic artery.

It may not be amiss at this time to review briefly the normal course of the ophthalmic artery. The internal carotid artery gives off its ophthalmic branch close to and behind the optic foramen, just where it makes its turn backward to enter into the make-up of the circle of Willis. The ophthalmic artery enters the optic foramen at the lateral and inferior surface of the optic nerve, making the nerve vulnerable to the pressure of an enlarged artery. In the orbit the vessel bends rather abruptly upward and then takes a course transversely between the nerve and the

24. Beadles, Cecil F.: Brain **30**:285, 1907.
25. Harkness: Internat. J. Med. & Surg. **43**:243 (May) 1930.

superior rectus muscle before it passes forward. Enlargements of the artery occurring coincidentally with involvement of some of the larger intracranial vessels have been found before its entrance into the orbit and also within the orbit. It may be noted that the intracranial portion of the ophthalmic artery is anterior to the motor nerves of the eye and thus could hardly obtain sufficient proportions to encroach on the nerves and cause ocular palsies. A distended artery within the orbit could obviously bring about motor disturbance only by direct mechanical interference with muscle activity, as in the case herein reported. Thus it becomes evident that a clinical diagnosis of true uncomplicated aneurysm of the ophthalmic artery, regardless of whether it is situated within the orbit or within the cranium, is practically impossible. Although the seat of the lesion may be placed with a degree of certainty, the nature of the lesion must remain in doubt, and the final analysis in these cases will have to rest on exploratory craniotomy.

NEOSYNEPHRIN HYDROCHLORIDE

SOME USES AND EFFECTS IN OPHTHALMOLOGY

PARKER HEATH, M.D.
DETROIT

The sympathomimetic compound neosynephrin hydrochloride has properties of interest to ophthalmologists. After three years of clinical trial and some experimentation on animals, a report is given under the following headings: (1) the general action of the preparation, (2) its local action and (3) some of its uses in ophthalmologic practice.

Neosynephrin hydrochloride has been accepted by the Council on Pharmacy and Chemistry of the American Medical Association, and its description is given in "New and Nonofficial Remedies."

GENERAL ACTION

There have been a considerable number of reports on the general actions of the drug. When it is given in rather small doses the blood pressure is raised and sustained over a considerable time. A dose of 1 mg. will produce in a few minutes a sustained rise of the blood pressure, whether the drug is given intravenously (an immediate effect), subcutaneously or intramuscularly, the ratio of the activity on the blood pressure of atropinized cats of the hydrochloride salt to that of epinephrine chloride being 4:3 (Tainter and Stockton [1]). The mechanism of the pressor action is said to be both musculotropic and neurotropic (Tainter and Stockton [1]). The drug is not as strong a bronchodilator as epinephrine hydrochloride, the ratio of its activity in this respect to that of epinephrine hydrochloride being 20:4 (Tainter, Pedden and James [2]). Nathanson [3] found a ratio of activity of 1:100 between epinephrine hydrochloride and neosynephrin hydrochloride in induced cardiac standstill. Studies on animals have shown some increase

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This is a preliminary report of a study undertaken for the Committee on Standardization of Drugs and Instruments, Section on Ophthalmology of the American Medical Association.

1. Tainter, M. L., and Stockton, A. B.: Am. J. M. Sc. **185**:832, 1933.

2. Tainter, M. L.; Pedden, J. R., and James, M.: J. Pharmacol. & Exper. Therap. **51**:571, 1934.

3. Nathanson, M. H.: Further Observations on Effect of Drugs on Induced Cardiac Standstill: Effect of Epinephrine and Related Compounds, Arch. Int. Med. **54**:111 (July) 1934.

in the blood sugar content following the use of neosynephrin hydrochloride and an increase in secretion of saliva and urine has been demonstrated (Geiter [4]). The lethal dose for animals is comparatively high. The toxicity varies with different species. The minimum lethal dose of ephedrine sulfate and of epinephrine chloride is much smaller than that of neosynephrin chloride. This dose is : for rats, from 0.7 to 0.8 Gm. per kilogram of body weight, administered orally; for rabbits, from 0.015 to 0.025 Gm. per kilogram of body weight, administered orally; for pigeons, 2.45 Gm. per kilogram of body weight, given subcutaneously or 0.0333 Gm. given intravenously (Geiter [4]). Barger and Dale [5] have shown that the sympathetic stimulation of substances like epinephrine hydrochloride increased with the chemical resemblance to that substance but that other effects than the pressor reactions were not necessarily consistent. According to the results of studies on animals, neosynephrin hydrochloride does not diminish allergic reactions.

LOCAL ACTION

1. The preparation has a marked decongestive effect. Tainter and Stockton [1] demonstrated in rabbits an antiedema effect of synephrin hydrochloride after a subcutaneous injection which produced a lessened reaction to mustard oil applied in the conjunctival sac, compared with the reaction in controls. I have observed this and also a similar delay in reactions when the drug was given by two other routes. After both subconjunctival injections of neosynephrin hydrochloride (in a 0.5 per cent solution) and its topical application (in a 1 per cent solution) a delay and a diminution in the reaction from the conjunctival application of ethylmorphine hydrochloride powder have been observed. Slit lamp examinations of the limbic vessels showed a marked sustained vasoconstrictor effect from the topical or subconjunctival injection of a 1 to 0.5 per cent solution of neosynephrin hydrochloride. Constriction begins in from thirty to ninety seconds and lasts from two to six hours.

2. The mydriatic effect is substantial with the 1 per cent solution. This varies somewhat, depending on how the solution is applied, but the dilatation is fairly uniform if the preparation is applied within a petrolatum ring on the cornea. The effect is noted in approximately ten minutes and lasts a variable length of time following a single instillation. The dilatation is uniform in various segments of the iris but is variable as to degree. In a series of several hundred eyes those with an intra-ocular tension in higher brackets (from 25 to 29 mm. [Schiötz])

4. Geiter, C. W.: Unpublished studies on neosynephrin chloride.

5. Barger and Dale: J. Physiol. **41**:19, 1910.

dilate more widely than those with an intra-ocular tension in lower brackets (from 15 to 20 mm. [Schiötz]). The pupil usually but not always reacts to light at the height of the dilatation. The dilatation lasts from ninety minutes to four and one-half hours. Some persons are especially susceptible, and in these the dilatation may last from six to eight hours. The latter group is very small. The dilatation of the iris is opposed by either physostigmine or pilocarpine hydrochloride, the first in a 0.2 per cent solution of the hydrochloride and the latter in a 1 per cent solution. The decongestive effect may be elicited without dilation of the pupil if neosynephrin hydrochloride is combined with a miotic.

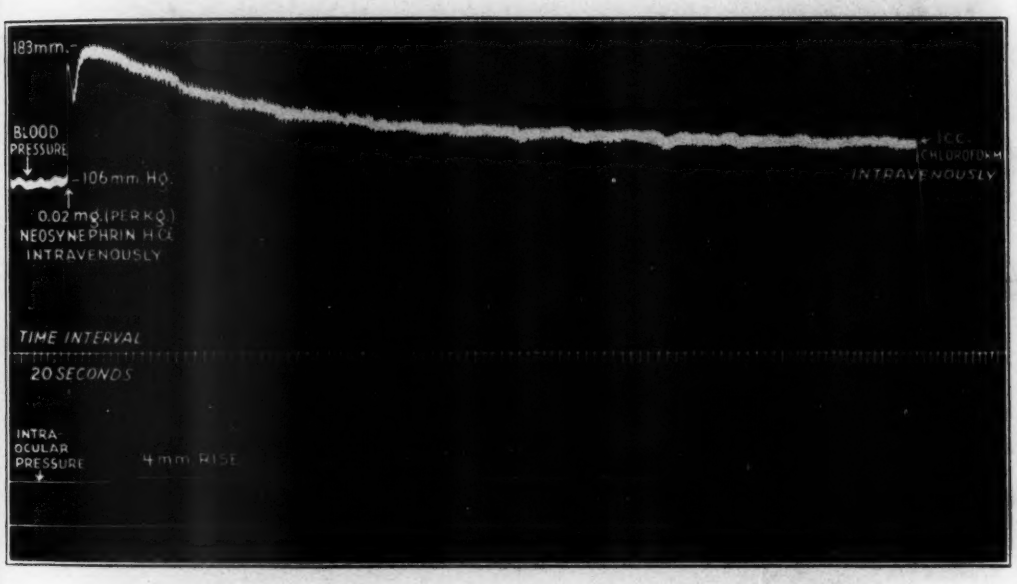

Fig. 1.—Mercury manometer record showing effect of neosynephrin hydrochloride (given by the intravenous route) on the blood pressure and the intra-ocular pressure of a male dog weighing 12.4 Kg., under anesthesia produced by sodium phenobarbital chloretone. Two-hundredths milligram of neosynephrin hydrochloride per kilogram of body weight was given. There was an abrupt rise of 77 mm. of mercury in the blood pressure and a rise of 4 mm. in the intra-ocular pressure.

3. A single instillation of a 0.5 to 0.75 per cent solution has little effect on the power of accommodation other than that resulting from the dilatation of the pupil. Repeated instillation has a mild cycloplegic effect. The partial loss of accommodation is of short duration, from two to ten hours, and follows the instillation of from 4 to 6 drops. This effect is opposed by physostigmine or pilocarpine hydrochloride.

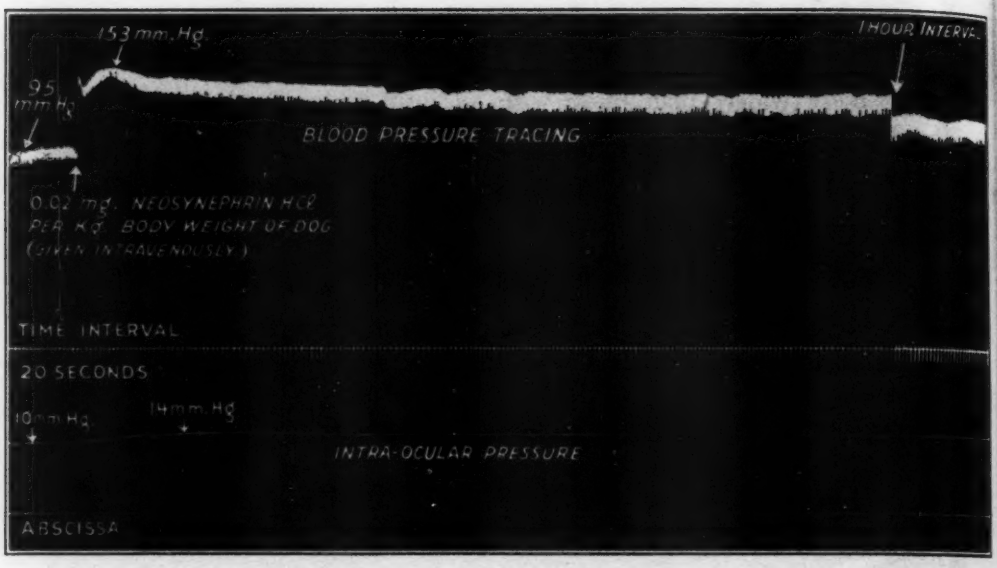

Fig. 2.—Mercury manometer record showing effect of neosynephrin hydrochloride (given by the intravenous route) on the blood pressure and the intra-ocular pressure of a male dog weighing 13.6 Kg., under anesthesia produced by sodium phenobarbital ether. Two-hundredths milligram per kilogram of body weight was given. There was an abrupt and sustained rise of 58 mm. of mercury in the blood pressure and a rise of 4 mm. in the intra-ocular pressure.

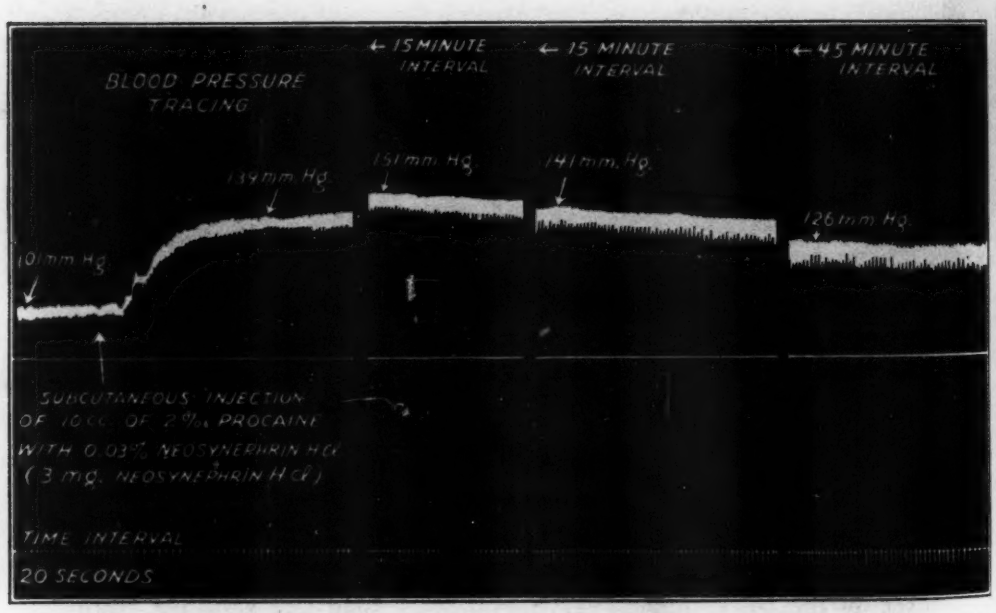
← 15 MINUTE INTERVAL
← 15 MINUTE INTERVAL
← 45 MINUTE INTERVAL
BLOOD PRESSURE TRACING
139 mm. Hg.
151 mm. Hg.
141 mm. Hg.
126 mm. Hg.
101 mm. Hg.
SUBCUTANEOUS INJECTION OF 10 CC. OF 2% PROCAINE WITH 0.03% NEOSYNEPHRIN HCl (3 mg. NEOSYNEPHRIN HCl)
TIME INTERVAL
20 SECONDS

Fig. 3.—Mercury manometer record showing the effect of neosynephrin hydrochloride (given by the subcutaneous route, as in local infiltration anesthesia) on the blood pressure of a male dog weighing 13.6 Kg., under anesthesia produced by sodium phenobarbital ether. Ten cubic centimeters of a 2 per cent solution of procaine hydrochloride combined with a 0.03 per cent solution of synephrin hydrochloride (3 mg.) was given. The rise in the blood pressure was more gradual than that produced by neosynephrin hydrochloride (50 mm. of mercury) alone and was long sustained.

4. A single topical application of a 0.5 to 1 per cent solution does not cause an increase of the intra-ocular pressure of a significant amount in many trials. In some patients repeated instillations (from 4 to 6) of a 1 per cent solution have produced a slight increase in the intra-ocular pressure. From intravenous use, coincidentally with a rise in the blood pressure (a dose of 0.02 mg. per kilogram of body weight in the dog) there has been a lesser rise in the intra-ocular pressure, as shown in figure 1. Pure neosynephrin hydrochloride (3 mg.) applied to the cornea of the dog produces the marked rise in the blood pressure noted in figure 4.

5. Neosynephrin hydrochloride will produce a pressor response in animals when the sympathetic nerve endings have been paralyzed after

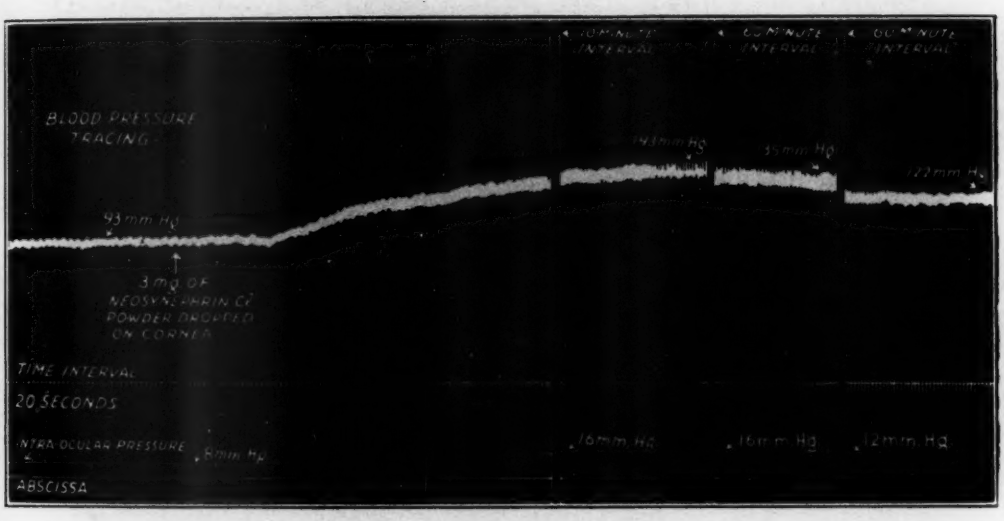

Fig. 4.—Mercury manometer record showing effect of neosynephrin hydrochloride (given through the cornea) on the blood pressure and the intra-ocular pressure of a male dog weighing 12 Kg., under anesthesia produced by sodium phenobarbital ether. Three milligrams of neosynephrin hydrochloride powder was given. The blood pressure rose to 50 mm. of mercury, and the intra-ocular pressure rose to 8 mm.; both these rises were gradual and sustained.

administration of ergotamine. It is thought accordingly that the compound acts on both the myoneural junction and the muscle. It obviously stimulates the dilator fibers of the iris. The dilatation of the pupil produced by the topical application of a 4 per cent solution of cocaine hydrochloride is increased by the further application of neosynephrin hydrochloride.

6. Interstitial injection of the compound as in local anesthesia produces marked ischemia and prolongs the local anesthesia caused by

procaine hydrochloride to about twice the normal length of time. In this regard it is about two-thirds as strong as epinephrine hydrochloride (a 1:1,000 solution). From 2 to 4 minims (0.1 to 0.2 cc.) of a 1 per cent solution of neosynephrin hydrochloride was added to 2cc. of 1 per cent solution of procaine hydrochloride. No side-effects have been noted such as have been seen in the use of epinephrine hydrochloride.

SOME USES IN OPHTHALMIC PRACTICE

Neosynephrin hydrochloride would seem to have definite advantages in practical use by the ophthalmologist:

1. For decongestion or as a vasoconstrictor a 0.12 to 0.25 per cent solution instilled into the conjunctival sac or a 0.5 to 1 per cent solution combined with a 0.125 to 0.25 per cent solution of pilocarpine hydrochloride may be used.

2. To dilate the pupil for intra-ocular examination one instillation of 1 minim (0.66 + mg. of the drug) of a 0.75 to 1 per cent solution may be used.

3. To prolong local anesthesia and to reduce hemorrhage in the field of operation a 1 per cent solution of procaine hydrochloride and a 0.025 to 0.03 per cent solution of neosynephrin hydrochloride may be used.

4. To dilate the shrinking pupil of a person with uveitis a 1 per cent solution may be used combined with atropine applied to the cornea. I have used pure neosynephrin hydrochloride powder (from 1 to 1.5 mg.) applied above the limbus to break synechiae, with considerable success, provided the adhesions have not been of too long a duration. This method has broken synechiae and given round pupils which had been resistant to the use of the repeated application of a 2 per cent solution of atropine and a 1:1,000 solution of epinephrine hydrochloride. No untoward action has been noted in six cases of severe uveitis in which the powdered form of the drug was used. In view of the experimental sharp rise of the blood pressure resulting from the application of the pure drug on the cornea, its use in this strength should be limited to cases of active uveitis in patients not afflicted with either severe arteriosclerosis or hypertension (fig. 5).

5. The drug has some value in a few selected cases for classifying patients with a high borderline intra-ocular pressure. Following dilatation produced by 1 drop of a 1 per cent solution of neosynephrin hydrochloride on the cornea (this may be quickly overcome by a miotic), a significant rise in the pressure would suggest a preglaucomatous state in the patient. Contrariwise, a significant fall of the intra-ocular pres-

sure would give a hint that the suspected glaucoma was of the secondary type. The classification is not as simple as appears from these statements, since a number of factors are involved, particularly the state of the capillary bed and the structure of the filtration angle.

6. The hemodynamic quality of this substance is of value in the treatment of shock and has been used clinically by Johnson.[6] The dose is from 5 to 10 mg. subcutaneously, or 3 mg. intravenously.

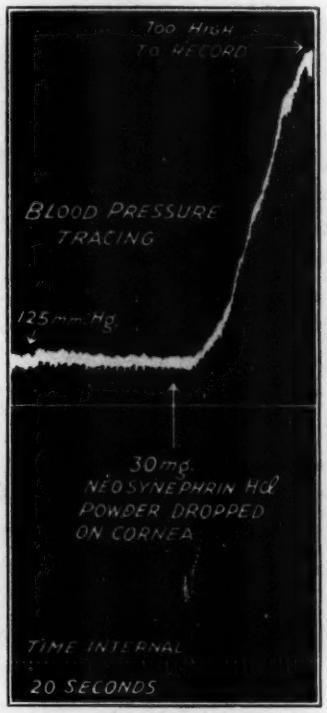

Fig. 5.—Mercury manometer record showing abrupt rise in the blood pressure in a dog after 30 mg. of neosynephrin hydrochloride powder was applied to the cornea. The recording limit of the mercury manometer was reached.

SUMMARY

A clinical and experimental study comparing neosynephrin hydrochloride with epinephrine hydrochloride and ephedrine hydrochloride in ability to contract capillaries is described. The general effects of the drug are discussed, and a report is given of infiltration anesthesia and of a clinical study of pupillary changes and changes in accommodation resulting from its use. Study of the perfused eyes of animals showed need for some care in the use of the preparation in pure form

6. Johnson, C. A.: Surg., Gynec. & Obst. **63**:35 (July) 1936.

in patients with arteriosclerosis and hypertension. The drug is useful to ophthalmologists to dilate the pupil for examination of the fundus (a drop of a 1 per cent solution), to break synechiae in cases of uveitis with adhesions of the iris and in cases of shock; it is of some value in differentiating various kinds of glaucoma and as a decongestive agent and a vasoconstrictor in the conjunctival sac.

Dr. C. W. Geiter gave assistance in the studies on animals.

EARLY OCULAR COMPLICATIONS OF EPIDEMIC MENINGITIS

N. K. LAZAR, M.D.
CHICAGO

The clinical observations which I am about to report, although rare, take on a definite importance when one considers the gravity of the complications of epidemic meningitis. It has been known for some time that a statistical study of any one epidemic, no matter how large a number of cases has been observed, will not give a true picture of the incidence of the complications. The geographic location, the severity of the epidemic, the type of organism and many other factors are involved, which are so variable that one cannot draw accurate conclusions. This is especially evident when one considers the literature. Epidemic meningitis appears to be on the increase throughout the United States.

Weed and Wegefarth [1] in 1914-1915 by their work on the relation of the spinal fluid and the intra-ocular fluids showed conclusively that a certain balance is maintained and that when this balance is disturbed in the presence of septicemia an infection in the eye results. This is an important consideration, as it will be shown that the opening of an eye in the presence of meningococcemia may produce a purulent infection in the eye. Curran [2] in 1915 reported the intra-ocular injection of antimeningococcus serum in a case of ocular infection complicating epidemic meningitis. There was some improvement in the ocular condition, although he did not state the extent of the improvement. Other investigators [3] have attempted the instillation of antimeningococcus serum into the conjunctival sac in such cases, with end-results which appear to be questionable. This is to be expected if the work of Ferry [4] and his co-workers is to be taken into consideration. They, as well as

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From the departments of ophthalmology of Northwestern University and Cook County Hospital.

Read before the Section on Ophthalmology at the Eighty-Seventh Annual Session of the American Medical Association, Kansas City, Mo., May 14, 1936.

1. Weed, L. H., and Wegefarth, P.: J. M. Research **25**:17, 1914; **28**:320, 1917.

2. Curran, E. J.: J. Kansas M. Soc. **26**:306, 1926.

3. Zarzycki, P.: Bull. Acad. de méd., Paris **78**:748, 1917.

4. Ferry, N. S.: J. Immunol. **23**:315 and 325, 1932; **26**:133, 1934.

Hoyne [5] and Herrick,[6] came to the conclusion that epidemic meningitis is a toxemia and must be treated as such. Ferry isolated the toxin and from it was able to produce an antitoxin, which has proved of great value in the treatment.

Bacteriologically, the organism has been recovered from the conjunctival sac and within the eyeball by Axenfeld [7] and McKee.[8] Uthoff,[9] however, was not successful in recovering the organism from the vitreous in three cases. This is explained by the well known fact that the organism does not remain in the tissues long after the onset of the coccemia.

There are few reports in the literature on the microscopic changes in the complications of epidemic meningitis. This is not surprising, because a study of endophthalmitis, for example, shows nothing characteristic of the disease or its complications. Collins and Mayou [10] reported the microscopic examination of an eye in which an embolus was observed lodged in the ciliary body. Axenfeld [7] stated the belief that the process starts in the retina and choroid and finally involves the vitreous. The optic nerve is involved secondarily. If one could procure an eye for microscopic study immediately after involvement instead of waiting until the process has become chronic, as is usually the case, something of value might be obtained from such a study.

A complete review of the literature has not been attempted in this paper, as this has been well done by Dunphy.[11] Nearly every tissue of the eye may become involved as a complication of epidemic meningitis, but within the past few years my associates and I have observed the intra-ocular and muscular complications only.

In 1933 I became interested in this subject because of the large number of patients that we were asked to see at the unit for patients with contagious disease of the Cook County Hospital. It was thought worth while to report these observations, the type of treatment employed and the introduction of a new medicament which has reduced the number of complications considerably.

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5. Hoyne, A. L.: Meningococcic Meningitis: A New Form of Therapy, J. A. M. A. **104**:980 (March 23) 1935.

6. Herrick, W. W.: Early Diagnosis and Intravenous Serum Treatment of Epidemic Cerebrospinal Meningitis, J. A. M. A. **71**:612 (Aug. 24) 1918.

7. Axenfeld, T.: Die Bakteriologie in der Augenheilkunde, Jena, Gustav Fischer, 1907.

8. McKee: Ophth. Rec. **17**:438, 1908.

9. Uthoff, W.: Ber. ü. d. Versamml. d. ophth. Gesellsch. **32**:84, 1906.

10. Collins, E. T., and Mayou, M. S.: Pathology and Bacteriology of the Eye, Philadelphia, P. Blakiston's Son & Co., 1911.

11. Dunphy, E. B.: Ocular Complications of Cerebrospinal Meningitis, Arch. Ophth. **15**:118 (Jan.) 1936.

For the sake of clearness I have divided these complications into intra-ocular and neuromuscular. In 1933 I observed (see table) 33 ocular complications of major importance in a total of 266 cases.

During the early part of this year it had been customary to inject the antimeningococcus serum intraspinally only. This in a measure may have accounted for the large number of ocular complications seen during this period. About the middle of March 1933 this procedure was changed, so that on admission the patient received the serum intravenously in much larger quantities. From then on during 1933 the number of ocular complications was reduced considerably. It was observed that most of the patients with the complication of paresis of the external rectus muscle still had the paresis on discharge from the hospital. Some of these patients were later observed in the clinic for

Ocular Complications of Epidemic Meningitis Observed in 1933, 1934 and 1935

Condition	Number of Cases		
	1933	1934	1935
Total number of cases of meningitis	266	98	211
Total number of ocular complications	33	6	5
Bilateral endophthalmitis	7	1	1
Endophthalmitis of the right eye	3	2	3
Endophthalmitis of the left eye	11	0	0
Panophthalmitis	1	1	0
Total number of cases of paresis of the sixth nerve	11	2	1
Right	5	1	1
Left	5	1	0
Bilateral	1	0	0

patients with diseases of the eye. The paresis cleared up completely. It was our experience at this time and for a long time prior to this study that when epidemic meningitis was complicated by endophthalmitis the eye was lost. The aforementioned observations should be kept in mind for the sake of comparison with those made in 1934 and 1935.

During 1934, among 98 patients with epidemic meningitis, 6 with ocular complications were observed. It was at the beginning of this year that Hoyne introduced the meningococcus antitoxin for treatment. Every third patient received the antitoxin by vein. Aside from the fact that the epidemic was mild as compared to that of 1933, none of the patients who received the antitoxin showed intra-ocular complications. Those receiving the serum did, as shown by the table.

During 1935 I observed 5 ocular complications in 211 cases of epidemic meningitis. Most of the patients were then receiving the antitoxin intravenously, and a few spectacular recoveries from intra-ocular complications were observed. The following 2 cases appeared to be proof of the efficacy of the antitoxin treatment.

REPORT OF CASES

CASE 1.—J. T., a youth 16 years of age, was brought to the hospital with severe meningococcic meningitis of twenty-four hours' duration. Both eyes showed a hazy anterior chamber and a very cloudy vitreous. The red reflexes were faulty, and beginning bilateral endophthalmitis was diagnosed. The patient was given meningococcus antitoxin. The following day both eyes had cleared considerably. The anterior chambers were clear; the vitreous had several floaters. The details of the fundus were visible. Two days later the eyes appeared perfectly normal, and the fundus was normal in both.

CASE 2.—A white boy 3 years of age was taken sick three days prior to admission with what appeared to be an infection of the upper respiratory tract. The mother stated that the night before the child had a high temperature, was stuporous and had a few red spots over his body. He was admitted to the unit for patients with contagious disease as having severe meningococcemia. On examination it was found that both eyes had beginning endophthalmitis. The right eye had no red reflex; the anterior chamber was cloudy, and the iris was muddy. There was little circumcorneal injection. The left eye had much more circumcorneal injection; the anterior chamber was cloudy, and the vitreous had many floaters. A few vessels of the fundus could be seen. On the day of admission the patient was given meningococcus antitoxin intravenously. Two days later the left eye had cleared up sufficiently so that the details of the fundus could be made out. The vitreous had a few floaters. The right eye never cleared sufficiently to enable one to see the details of the fundus. The nasal side of the right eye had a red reflex, but the temporal side was dark. This patient received, in addition to the antitoxin, intramuscular injections of milk and subconjunctival injections of mercuric oxycyanide in a 1:5,000 solution. The right eye, when last seen in December 1935, appeared to be shrinking. The left eye was normal.

From the observations just reported there appears to be no doubt that ocular complications of epidemic meningitis are due to an infection of the blood stream. As further proof the 2 additional cases are cited.

CASE 3.—A Negro girl 2 years of age was brought to the hospital because of an apparent ocular infection. The informant said that the mother and another child in the family were in the unit for patients with contagious disease with meningitis. On examination it was found that the baby had endophthalmitis of the right eye. Otherwise the examination gave negative results. Meningeal symptoms were absent. The patient was admitted to the unit for patients with contagious disease with a diagnosis of epidemic meningitis. Examinations of the spinal fluid and blood both showed the meningococcus. The child was discharged two weeks later. The eye was lost.

CASE 4.—A 3 year old white child was admitted to the Children's Hospital because of a diagnosis of infection of the upper respiratory tract and iritis. Examination of the eye revealed endophthalmitis in the left eye. All the other symptoms cleared up within forty-eight hours. Examination of the spinal fluid and blood did not show the meningococcus. There was no history of meningitis in the family, but my associates and I were told by the physician who had seen the patient prior to admission that the child had what he thought was meningitis.

Cases of endophthalmitis apparently due to the meningococcus in patients without meningitis have been reported by McKee and others.

Cultures were made from the vitreous and aqueous of 3 patients. No positive cultures were obtained. Axenfeld,[7] McKee [8] and others have recovered the organism from such materials.

Early in 1933 an attempt was made to remove some vitreous from the eyes of patients with endophthalmitis and replace it with a small amount of antimeningococcus serum. Panophthalmitis developed in one case, and in the second case no changes in the condition were apparent. I do not believe that any method which has for its purpose the injection of material into an eyeball for the treatment of complications of epidemic meningitis will be successful.

During the past year my associates and I obtained two of the eyes which were observed. These were enucleated at the Cook County Hospital, and sections were made by the Northwestern University Eye Clinic. These were studied by Dr. Beulah Cushman, and her report is as follows:

CASE 1.—*Clinical History.*—J. S., a Negro aged 10, had epidemic meningitis in May 1934, complicated with endophthalmitis of the right eye, with subsequent loss of vision and shrinking of the eye. The eye was enucleated in April 1935.

Microscopic Examination.—Cornea: The stroma was infiltrated posteriorly, and in some areas Descemet's membrane had disappeared with the endothelium. There was increased vascularization of the limbic areas.

Anterior Chamber: The anterior chamber was shallow and was filled with a lymphocytic infiltration, pigment and new fibrous tissue. Epithelioid cells were present.

Iris: The iris was diffusely infiltrated with lymphocytes and migratory pigment and was adherent to the capsular epithelium.

Ciliary Body: There was a dense vascularized membrane of the ciliary processes, and with the detached retina these formed a mass which showed marked hyalinization, gliosis and migration of pigment.

Lens: The lens was cataractous, with morgagnian globules under the posterior capsule. The choroid was adherent to the cyclitic mass in the area of the ora serrata; posteriorly on the right side there was a fresh large subchoroidal hemorrhage (operative). There was scattered lymphocytic infiltration in the region of the optic nerve.

Optic Nerve: The optic nerve was pulled forward with fibrous tissue proliferation. The nerve was irregular, and there was atrophy of a large portion of the fibers.

Sclera: The sclera was thickened and contracted.

CASE 2.—*Clinical History.*—John M., 10 years of age, had had epidemic meningitis in the spring of 1935 (the month was not given), complicated with meningococcic endophthalmitis of the right eye, and he had a shrunken eye following this. He was admitted on Aug. 12, 1935. The right eye was enucleated, and he was discharged on August 17.

Microscopic Examination.—Cornea: The epithelium and Bowman's membrane were intact. The cornea was contracted irregularly, and there was increased infiltration at the angles. There was diffuse infiltration posteriorly, with anterior adhesions of the iris in the pupillary area and scattered discrete anterior adhesions. Descemet's membrane was irregular in the central area, with infiltration into the

stroma and loss of the endothelium, to which a dense fibrous and vascularized pupillary membrane was adherent, extending to the capsule of the lens, which had been detached.

There was fresh hemorrhage between the capsule of the lens and the pupillary membrane (operative). There were scattered lymphocytes in the aqueous and on the posterior surface of the cornea.

Iris: The iris was adherent to the pectinate ligament on both sides as far as Descemet's membrane and was displaced forward. There were scattered anterior adhesions and scattered lymphocytes and plasma cells in the iris. The posterior pigment layer was adherent to the capsule of the lens. The sphincter stained well throughout.

Ciliary Body: The circular muscles were pulled axially. There was a loss of practically all the unpigmented epithelium from the ciliary processes, and on the left side at the base of the circular fibers there was a formation of small round cells but no giant cells. On the right side there was a diffuse hemorrhage in the longitudinal fibers of the ciliary body, with scattered fine pigment, macrocytes filled with pigment, fresh blood cells and scattered lymphocytes, extending posteriorly, with detachment of the choroid. There was scattered migration of pigment throughout the ciliary body. Ciliary processes were caught in the cyclitic membrane and, with the detached retina, were drawn axially.

Choroid: The subchoroidal hemorrhage on each side extended back to the equator. The dense cyclitic membrane and adherent ciliary processes with loss of unpigmented epithelium and distortion of the pigment epithelium were firmly adherent to the posterior capsule of the lens, and the umbrella-shaped detachment of the retina was caught in the same mass. There were scattered foci of small lymphocytes throughout the cyclitic membrane. There was one group of epithelioid cells in the central portion of a group of round cells. There was a recent fibrous membrane extending between the choroid and the retina in the vicinity of the optic disk. The choroid in the equatorial region was drawn axially, with migration of pigment extending along the fibrous tissue. In the choroid on the right side of the optic nerve there were foci of lymphocytes.

Retina: The retina was detached, markedly degenerated and surrounded by a vascularized cyclitic membrane.

Optic Nerve: The fibers of the disk were drawn axially by the detachment; there was increased cellular infiltration, and round cells were present about the central artery. There was cellular infiltration of the meningeal coats; the arachnoid and pia were adherent, with new fibrous tissue formation, and in some areas the spaces were completely blocked. There was only a small amount of nerve tissue remaining in the nerve head and extending posteriorly through the lamina cribrosa.

Sclera: The sclera was distorted and drawn toward the axis of the eye in the region of the equator. There was moderate episcleral perivascular infiltration.

Special Stains: With the Weigert and Van Gieson stains there was bright red stained connective tissue in the cyclitic membrane and in the detached axially drawn choroid. Loss of nerve fibers was observed.

COMMENT

It will be noted from the pathologic reports just cited that one can draw no conclusions as to the pathogenesis of complications of the posterior segment except that the infection evidently reaches that segment through the retinal or choroidal vessels, or both. It might be

of value to study serially cases in which the eye was enucleated not more than twenty-four hours after involvement. According to Axenfeld and other investigators, the process begins in the retina and choroid and then spreads to the vitreous, forming an abscess. The optic nerve is involved secondarily.

TREATMENT

For the sake of completeness, the treatment of the disease will be given; for a detailed description the reader is referred to Hoyne's paper.[5] Infants up to 2 years of age are given 50,000 units of meningococcus antitoxin in a 10 per cent solution of dextrose and sodium chloride, by vein. This is repeated two or three times once in twenty-four hours, if necessary. To children over 6 years of age, usually 100,000 units, and sometimes from 60,000 to 80,000, is given intravenously. As a local measure a 1 per cent solution of atropine sulfate is instilled into the eye three or four times daily. If conjunctivitis is present a mild antiseptic is employed. In several cases, about two to three days after involvement, injections of a 1:5,000 solution of mercuric oxycyanide were given under the conjunctiva, but no effect was noticeable. Foreign protein, such as typhoid vaccine containing from 25,000,000 to 50,000,000 organisms, was given intravenously, with no noticeable change in the condition.

CONCLUSIONS

Epidemic meningitis is accompanied by toxemia.

During 1933, 1934 and 1935 two major ocular complications have been observed in association with epidemic meningitis, namely, endophthalmitis and paresis of the external rectus muscles.

Treatment of the disease with an antitoxin has reduced greatly the number of ocular complications.

Local treatment is without avail, once the posterior segment has become involved. This is especially true when the serum is employed. In cases of endophthalmitis that is well developed the condition is not influenced by the use of antitoxin or foreign protein. Within the first one or two days of this complication the antitoxin seems to be of value, as shown in the cases here reported.

Microscopic examination in cases of endophthalmitis complicating epidemic meningitis shows nothing that distinguishes the condition from endophthalmitis due to other blood-borne infections.

55 East Washington Street.

ABSTRACT OF DISCUSSION

DR. ARCHIBALD L. HOYNE, Chicago: Dr. Lazar's paper is of unusual importance. Unless the ophthalmologist has some special association with a hospital for patients with contagious disease he rarely has an opportunity to observe the complications that have just been described.

Several factors in connection with meningococcic infections as they relate to complications should receive particular consideration. If meningococcic meningitis is primarily an infection of the blood stream, this fact will have a distinct bearing on the mode of treatment. Whether the symptoms are due chiefly to toxemia or whether they result from bacterial invasion which causes suppurative conditions should have an influence on the method of treatment.

For many years serum therapy has been directed primarily against the organisms, and therefore the intraspinal route for the administration of serum has often been used to the exclusion of all other routes.

Among a series of 233 patients with meningococcic meningitis treated by serum given intraspinally at the Chicago Municipal Contagious Disease Hospital prior to 1936, in 17 instances vision was lost in one or both eyes. In other words, ocular complications which involved the loss of sight occurred in 7.2 per cent of the cases. In some instances panophthalmitis or endophthalmitis developed extremely early in the course of the disease, while in others such complications came on after the patient had recovered from meningitis.

My associates and I have found that with massive doses of antimeningococcus serum or Ferry's meningococcus antitoxin given intravenously few suppurative complications occur. In respect to the eye, when loss of vision is involved, the complication that develops may be endophthalmitis, but with the present form of treatment panophthalmitis is almost unknown.

My associates and I have now treated more than 300 patients with Ferry's meningococcus antitoxin given by the intravenous route and have not yet observed a single instance in which loss of vision occurred in any patient after this form of treatment was commenced. The same statement, however, has not held true for antimeningococcus serum, for even though the patient has appeared to be making satisfactory progress endophthalmitis has sometimes developed during convalescence.

As Dr. Lazar pointed out, local treatment for ocular conditions in patients with meningococcic meningitis seems to be of no avail. However, on two or three occasions large doses of Ferry's meningococcus antitoxin administered intravenously did not seem to be beneficial in cases in which endophthalmitis was already present.

Dr. Parker Heath, Detroit: One agrees with the author that clinical complications statistically studied vary in different reported epidemics. This is in part due to different observers and strains of organisms and especially to variation in the time of diagnosis and treatment. The time element is a principal factor, since early complications are more variable and late complications tend to remain fixed.

The author's paper is concerned with two early ocular complications, specifically, endophthalmitis and transitory paresis of the sixth nerve. These two complications are used as a gage in comparing the severe 1933, the milder 1934, and the severe 1935, Chicago epidemics and evaluating the results of Ferry's antitoxin used intravenously. Dr. Lazar reported marked benefit following the use of antitoxin administered intravenously. If other clinical reports agree with this the value of specific antitoxin will be established. Then these brilliant clinical results may be said to be consistent with the lessening of complications

after use of similar antitoxins in other diseases, as in diphtheria. Early diagnosis and treatment would seem to be the crux of success in a lowered incidence of complications and a lowered mortality.

It is too early to establish whether the better method of treatment is that in which intravenous injections are used or that in which intravenous injections are combined with intraspinal injections.

Dr. Lazar tried intravitreous treatment, using antimeningococcus serum (the amount was not stated) in two eyes, and, unlike Netter and Curran, has reported no benefits.

Dr. Beulah Cushman's study of the two eyes enucleated because of meningococcic endophthalmitis, as the author justly stated, was made too late in the pathologic process to enable her to describe and localize the primary lesion. As to the ocular source of the lesion, I have been impressed in a considerable number of cases with a large exudation in the vitreous, apparently arising from the ciliary body.

It is to be hoped that further studies will include those of other common acute ocular complications, such as palsy of the third nerve, neuroretinitis, sudden and temporary blindness and, possibly, conjunctival lesions. The late residual complications are another story. The use of Ferry's antitoxin, as shown in Hoyne's series, lowers the mortality rate and does this in cases in which the course is not particularly favorable. The hope for reduction in the number of ocular complications as reported by Dr. Lazar should stimulate early treatment. In the presence of an epidemic, treatment of patients suspected of having the disease would seem to be logical.

Dr. Henry C. Haden, Houston, Texas: In 1917 I was called to see a boy about 15 years of age who had had an attack of endophthalmitis associated with epidemic cerebrospinal meningitis. His general condition had improved very much. He had been receiving intraspinal injections of the antimeningococcus serum, but the ocular complication developed. When I saw him the pupil was dilated, and I could see a white mass in the vitreous. In a few days after the administration of the antimeningococcus serum intravenously the white mass disappeared, but the patient's vision did not return. Subsequently the eye was removed, and a complete microscopic study was made of it.

This case was reported in the *American Journal of Ophthalmology* (1:647 [Sept.] 1918). My associates and I advocated at the time the intravenous use of the serum in such cases.

Dr. Albert H. Mann, Texarkana, Texas: During the past winter there was a minor epidemic of meningococcic meningitis in Texarkana. During this epidemic there were 10 cases, with 7 deaths—a mortality of 70 per cent. In these 10 cases there were 2 ocular complications. Both these patients recovered. The one eye was subsequently enucleated. The second eye was seen by me a few days ago and presented practically complete loss of vision. The tension was normal. There was a posterior synechia of the temporal half of the pupil, but the most interesting feature was a net of deep vessels in the cornea. The right cornea was normal, and there was no history of interstitial keratitis.

The appearance of the cornea on slit lamp examination was not that of syphilitic interstitial keratitis of long standing.

The high mortality and the high incidence of ocular complications are interesting.

DR. NATHAN K. LAZAR, Chicago: The number of cases that my associates and I observed in 1933 was 266; in 1934, 98, and in 1935, 211. Because of the large number of cases observed in the first part of 1934, we thought that there were going to be 600 or 700 cases for this year, but at the end of the year the number was only 98.

The cases in which there was bilateral endophthalmitis were interesting. In 1933 there were 7 cases of this condition, whereas in 1934 there was only 1 and in 1935 there was none. The paresis of the sixth nerve always cleared up; we never observed a case in which it did not.

I should like to report on some of the cases that we observed this year. There is a possibility of recurrence. We observed a boy who had endophthalmitis in the beginning and severe toxemia. He was given antitoxin. Two days later the eye was greatly improved; one could see the vessels in the fundus, and the boy could see. About seventy-two hours after admission the endophthalmitis recurred overnight, and the eye was lost. I do not know the explanation for this. I hoped that Dr. Hoyne would say something about it, because I do not like to leave the impression that antitoxin is 100 per cent efficacious. We have, however, seen spectacular recoveries take place at the unit for patients with contagious diseases such as have never occurred with serum treatment.

We always thought that once an eye became involved it could not recover. However, we have seen several cases in which the eye has cleared up with the use of antitoxin. We were unfortunate in not seeing patients who showed optic neuritis and other complications.

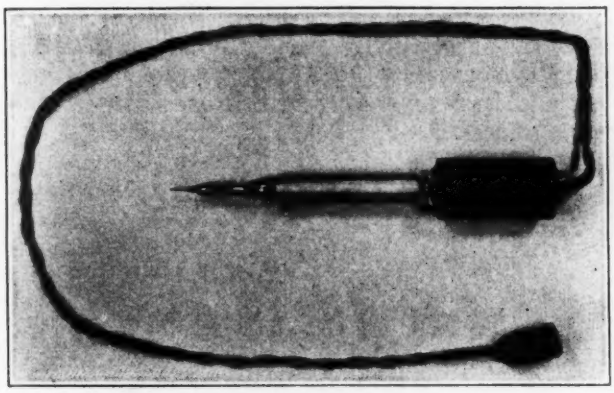
Clinical Notes

A NEW ELECTRIC CORNEAL DRILL

Louis A. Witzeman, M.D., Akron, Ohio

After being confronted repeatedly with the difficult task of removing particles of emery from the cornea, or of rust after a metallic foreign body had been removed from the eye, I became interested in finding a method for the removal of these particles that would be less traumatic to the delicate structures involved and at the same time would be less time consuming for the oculist.

After giving fair and reasonable trial to the many forms of instruments for the removal of such foreign bodies offered by the various



Electric corneal drill.

instrument houses today, it was decided that the bur used by the dentist was the most satisfactory tool for the purpose. However, such a bur is usually permanently attached in a handle, or a universal handle is provided in which various-sized burs can be introduced. In either case the handle is sufficiently large in diameter that an insufficient amount of speed can be obtained by twirling the instrument between the fingers in order to get the best results. Furthermore, the twirling motion made by the fingers is sufficiently unsteady to cause excoriation of an unnecessarily large area of the cornea.

In order to overcome these difficulties, I asked V. Mueller & Co., of Chicago, to substitute a chuck for the trephine on that most splendidly designed of instruments known as the Green corneal trephine. Into this chuck one can introduce any of the many burs that are made for the dental profession for the drilling of teeth. They are sharp and inexpensive and can be readily sterilized by any method desired.

The corneal drill uses as its source of power two ordinary 10 cent dry cells of the size used in a flashlight. Two cells have served me for about six months and are still far from a state of exhaustion. The drill is so held that it occupies a position approximately vertical to the surface of the cornea. A switch is conveniently situated, so that one can instantly and conveniently control the electricity with the index finger. The handle of the drill is light and well balanced, thus not interfering with delicacy of manipulation. The size of bur found most generally useful is the no. 1, short shank, although the no. 2, which is somewhat larger, is occasionally useful also. These sell for approximately 16 cents per half-dozen at most dental supply houses.

At first thought one might think that such an instrument would be prone to perforate the cornea. On the contrary, this is not the case. I am convinced that there is much less destruction of corneal tissue with its use. In fact, one can clean off a bulging Descemet's membrane with infinitely more safety than by the methods more commonly in vogue. Furthermore, there is no tendency for the electric drill to split the corneal layers as in the case with sharp hand-propelled instruments. Hence infection is less prone to occur.

In addition, with the use of this instrument, as checked by the slit lamp, there remains a definitely cleaner wound. Since less corneal tissue is removed, less débris is permitted to remain in situ and infection is less frequent and less corneal opacification results. Last but not least, I am sure that this improved result is obtained with the expenditure of a small fraction of the time formerly spent by the oculist.

News and Notes

SOCIETY NEWS

International Organization of the Campaign Against Trachoma.—The International Organization of the Campaign Against Trachoma was founded at the Thirteenth International Congress of Ophthalmology at Amsterdam in 1929. At the meeting in Geneva in 1930, which was attended by sixty-four delegates from thirty-two ophthalmologic societies, an executive committee for the organization was elected. The organization was founded for the following purposes:

1. To help in the collaboration of the different organizations which combat trachoma.

2. To work in concert with the International Organization of Public Health of the League of Nations.

3. To institute inquiries into the geographic distribution, the gravity and the sequelae of the disease.

4. To observe all measures relative to the activities to combat trachoma, to assist with these measures and to propagate a knowledge of them.

5. To organize meetings to consolidate the scientific bases of the campaign against trachoma, to elucidate the problems of its etiology, its fundamental causes, the diagnosis, the pathologic features, the therapeusis and the prophylaxis, as well as the scientific and social questions concerned, in order to propose the legislative measures which are indicated.

The scientific meetings of the organization are held annually in the spring and may be attended by any physician who becomes affiliated with the organization by the payment of an annual subscription of the exchange value of 10 Swiss francs (this fee is subject to change, owing to the uncertainty of the exchange). Reports of the scientific proceedings are published in the *Revue international du trachome*, a journal which is issued every three months, the subscription fee being 45 French francs.

The expenses of the International Organization of the Campaign Against Trachoma have been supported since its inauguration by donations from twenty of the national ophthalmologic societies. It is hoped that all who are interested in trachoma will send their subscriptions by a bank to the credit of the International Organization of the Campaign Against Trachoma, at the National Provincial Bank, 23 Wigmore Street, London, W. The subscription of the organization is 13 shillings, sterling; the combined subscription to the organization and the *Revue internationale du trachome* is 1 pound and 5 shillings, sterling.

Howe Medal Presented to Sir John Herbert Parsons.—At an informal meeting of the American Ophthalmological Society, held at the Waldorf-Astoria Hotel in New York on Tuesday, September 29,

the Howe Medal of the American Ophthalmological Society was presented to Sir John Parsons for his distinguished service to ophthalmology. About one hundred members of the society attended the meeting. Dr. F. H. Verhoeff, of Boston, who made the presentation for the society, said:

"Of the eight awards of the Howe Medal of the American Ophthalmological Society for distinguished service to Ophthalmology, three have been bestowed upon ophthalmologists of other countries. This year the Committee has unanimously decided to award the medal to another famous foreigner. Some men in their contributions to ophthalmology are noted for their ability to carry out original investigations, some for their ability to correlate the investigations of others so as to give the results greater meaning or importance. The ophthalmologist selected by the Committee is distinguished for his abilities in both these respects. His broad knowledge of science in general has enabled him to grasp in a comprehensive way the diverse problems with which he has dealt. In spite of his great achievements he has retained an innate modesty and freedom from pretense. His treatise on the 'The Pathology of the Eye,' completed twenty-eight years ago, has not been surpassed in its general treatment of the subject, and still remains the standard for reference. His treatises on other subjects set equally high standards. His writings are notable for their clarity. In only one volume, 'The Theory of Perception,' does the reader have any difficulty in following his line of thought, but no doubt this is due to the intricacy of the subject. As to some of his statements in this volume, I suspect he would admit, as did Browning in the case of some of his poems, that originally only God and himself knew the meaning, and that he has forgotten it. That the duty and privilege of presenting the medal on this occasion has fallen to me affords me especial satisfaction because I had the pleasure of observing and admiring the work of this scientist in the early stages of his career. As representative of the American Ophthalmological Society, I present for his distinguished service to Ophthalmology, the Howe Medal to Sir John Herbert Parsons."

Fifteenth International Ophthalmological Congress.—During the period of the Fifteenth International Ophthalmological Congress to be held in Cairo, Egypt, from Dec. 8 to 14, 1937, the International Organization of the Campaign Against Trachoma will hold scientific sessions, which will be open to all ophthalmologists. Reports will be presented on "The Microbiologic Etiology of Trachoma" and "The Pathology of Trachoma from Different Aspects."

The business session will be open only to annual subscribers to the International Organization of the Campaign Against Trachoma and to nominated delegates.

Complete information regarding presentation of papers may be obtained from Dr. Marx, the secretary general of the International Ophthalmological Congress, 316 Oostzeedijk, Rotterdam, Netherlands.

Philadelphia County Medical Society, Eye Section.—The Eye Section of the Philadelphia County Medical Society presented the following program at its scientific meeting on Oct. 8, 1936:

"Presentation of Cases with Fundus Changes Related to the Program Topics," by Dr. Roscoe J. Kennedy.

"Clinical Significance of Retinal Changes in Toxemias of Pregnancy." This was divided into "Ophthalmological Phases," by Dr. Glenn G. Gibson, and "Obstetrical Phases," by Dr. P. Brooke Bland.

"The Neurologic Aspects of Optic and Retrobulbar Neuritis," by Dr. Bernard J. Alpers.

The Société d'ophthalmologie de Paris.—The annual meeting of The Société d'ophthalmologie de Paris was held on Nov. 15, 1936. The following subjects were discussed: "Les hallucinations visuelles" by Dr. Baruk and "Corps flottants du vitre" by Dr. Jean-Gallois.

PERSONAL

Word has been received that Dr. Hermenegildo y Ricardo Arruga has escaped from Barcelona with his family and is now living in Toulouse. Dr. Ignacio Barraquer reached Marseilles in an airplane. Ophthalmologists in Madrid do not seem to be in danger.

GENERAL

American Board of Ophthalmology.—The American Board of Ophthalmology will conduct an examination at Los Angeles, Saturday, Jan. 23, 1937. All applications for this examination should be filed before Dec. 1, 1936, and case reports must be submitted before December 15. For further information, write to Dr. John Green, Secretary, 3720 Washington Boulevard, St. Louis.

CORRECTION

In the article entitled "Reaction of Buffer Solution and of Ophthalmic Drugs: A Further Note," by Dr. Sanford R. Gifford, in the January 1935 issue (**13**:78, 1935) "boric acid (anhydrous)" in the seventh line on page 79 should read "ordinary powdered boric acid."

Obituaries

CLAUD WORTH, M.D.

Claud Worth died on June 24, 1936. After receiving his medical degree from St. Bartholomew's Hospital, London, where he began the study of ophthalmology under Henry Power and B. Vernon, he became connected with Moorfields, where he worked under Holmes Spicer, and was elected an honorary member of the staff in 1906. He retired from practice in 1929.

He is best known by his interest in squint, and his book "Squint, Its Causes and Treatment" has reached its sixth edition and has been translated into many languages.

The orthoptic treatment of squint in young children was the subject of an article which appeared in volume 21 of the *Transactions of the Ophthalmological Society of the United Kingdom* in 1901. Worth's amblyoscope has been universally adopted.

According to Bishop Harman,[1] "Claud Worth was one of those unusual men who make their mark in two distinct spheres of life. In his earlier days, before success had come to him, he gave little, if any, indication to his colleagues of the powers that were in him. He was somewhat under middle height, slow and hesitant of speech, dapper, almost dandified in his dress, meticulous in procedure, and he gave the impression of a remoteness from the rough and tumble of practical everyday affairs that would seem to be certain to prevent his making any significant contribution to medical progress or human content. Yet he did a great work in the development of the systematic treatment of squint—one might almost say in initiating that treatment. For although some before him had conceived such possibility, experimented upon it, and given laborious days to the work, yet it was not until Worth had taken it in hand that there arose such interest as has led to the present-day formation of the orthoptic clinics, which are the recognized feature of so many eye hospitals and school treatment centres. Thirty or more years ago some of us were inclined to smile when we saw Worth shepherding a small flock of squinting children into a side room of the out-patient department of Moorfields. There, hour after hour, with laborious diligence he tried to persuade these restless imps to perform feats of mental and ocular gymnastics which we felt sure they did not want to do and which they could not do. But Worth with his gentle way, absence of fuss, quiet persistence, and even obstinacy, achieved

1. Claud Worth, Obituary, Brit. M. J. **2**:51 (July 4) 1936.

the seemingly impossible. Out of that work came his book on the treatment of squint—a small book as bulk in paper goes, but large in its effects. It has gone through six editions and is the basis of the many later books upon the subject of the orthoptic treatment of squint. Success did not change his gentleness and kindliness of character. Indeed he always gave something of the impression of diffidence, or even of withdrawal, which was in itself disarming to the most critical."

Apart from his important contributions to ophthalmology, he was especially interested in the science of sailing, became a master mariner and first-class pilot and was the author of several books on navigation which are classics.

ARNOLD KNAPP.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Anatomy and Embryology

THE INNERVATION OF THE HUMAN SCLERA. KARL A. REISER, Arch. f. Augenh. **109:** 481, 1936.

Little work has been done on the innervation of the sclera since that of Attias, Bach and Agababow, owing chiefly to the fact that it is difficult to obtain a differential stain of nerves embedded in connective tissue such as the sclera. Because of the dense felt work which the scleral fibers form it is nearly impossible to create teased dissections. Practically the only papers which have appeared in this interval deal with the occurrence of nerve loops in the sclera, the so-called Axenfeld loops.

Reiser reviews the general arrangement of these fibers as follows: A plexus of the first order is formed by nerve bundles of different size, similar to the nerve plexuses of the intestines. A secondary plexus, which he describes as a plexus of the second order, can be differentiated from this by the smaller caliber of its nerve bundles and the less frequent occurrence of medullated fibers. A preterminal network of from six to eight fibers comes from each bundle, which anastomose freely with each other. From this preterminal network a terminal reticulum spreads out in the form of a syncytium, spinning around the connective tissue cells of the sclera. Every fiber is surrounded by a sheath of Schwann.

F. H. ADLER.

Biochemistry

THE WATER-BINDING OF THE OPTIC NERVE AND OF ITS SHEATHS. J. A. VAN HEUVEN and P. F. FISCHER, Brit. J. Ophth. **20:** 204 (April) 1936.

After describing their experiments on the eyes of oxen to determine the capacity, intensity and form of the water-binding of the optic nerve and its sheaths van Heuven and Fischer state their conclusions: ". . . it is proved that these tissues have the possibility of swelling. The capacity and intensity of the water-binding of the optic nerve is much greater than that of the retina. Moreover, the water-binding of the optic nerve is of a different type from that of the retina. The conditions of water-binding are the same in the sheaths of the optic nerve as in the sclera. Furthermore the clinical significance of the water-binding of the optic nerve and its sheaths is discussed and some remarks are made on the theories of the genesis of papilloedema."

W. ZENTMAYER.

THE VITAMIN C CONTENT OF AQUEOUS AND ITS ANTISCORBUTIC ACTION. C. CELLA and I. D. GEORGESCU, Compt. rend. Soc. de biol. **121:** 1116, 1936.

The aqueous contains more vitamin C than any other fluid of the body. In cattle on the dry winter diet of hay and grain (which is prac-

tically free from vitamin C) the aqueous averages 20 mg. of cevitamic acid per hundred cubic centimeters as chemically determnied by Bezssonoff's technic. To verify biologically the antiscorbutic action of this aqueous, guinea-pigs maintained on a diet free from vitamin C for thirty days were given 10 cc. of it daily. According to the previous chemical determination, this contained 2 mg. of cevitamic acid, the amount required to protect a guinea-pig from loss of weight. Thirty days later the controls were dead, whereas the animals receiving the aqueous were healthy and without scurvy.

J. E. LEBENSOHN.

Color Sense

COLOR ASTHENOPIA: ITS EVALUATION AND DIAGNOSIS. A. Y. SAMOYLOV, Sovet. vestnik oftal. **8:** 1, 1936.

This is the first article on the subject to be published in Soviet Russia. The symptom complex of color asthenopia was first reported in 1933 by Engelking. The most important symptom is color fatigue, the presence of which is ascertained by Nagel's anomaloscope. The subject is allowed to look for half a minute only into the anomaloscope and to state the color equation; then he looks for a few minutes at an evenly illuminated surface (sky, snowy ground, green meadow), after which he looks again into the anomaloscope; if he accepts his previous color equation this is stated as his color vision. The results of the simple routine examination for color asthenopia Samoylov names "the swing" of the color equation. About 20 per cent of normal trichomats enlarge their initial color limits because of color fatigue. The basic symptom of color asthenopia is an absolute refusal to accept the initial color equation after the period of rest. Color asthenopia is observed among normal and abnormal trichomats. The diagrams show that the equations of the color asthenope coincide with those of the dichromat of either type—deuteranope or protanope.

The theoretical value of the study of color asthenopia is that it gives better understanding of the mechanism of color perception. The practical value is that it establishes the presence of color asthenopia under abnormal conditions in normal trichomats who are applicants for positions in railroading or in aviation; such applicants should be rejected, as they will not be able to distinguish colors when fatigued during work.

Six tables and two diagrams illustrate the article.

O. SITCHEVSKA.

Conjunctiva

STREPTOCOCCAL PSEUDOMEMBRANOUS CONJUNCTIVITIS. H. C. KLUEVER, Am. J. Ophth. **18:** 1094 (Dec.) 1935.

The following conclusions are given:

"1. Pseudomembranous conjunctivitis complicated by pseudomembranous vaginitis and acute glomerular nephritis persisted for 30 months and resulted in the loss of one eye.

"2. Streptococcus haemolyticus was repeatedly isolated from the pseudomembranes.

"3. Scarlet-fever streptococcal antitoxin exerted a favorable effect upon the disease.

"4. Subcutaneous administration of scarlet-fever streptococcal toxin, intradermal administration of autogenous streptococcal vaccine, and local application of filtered autogenous broth vaccine (Besredka) stimulated the formation of pseudomembranes.

"5. The lesions of the right eye and vagina healed after attempted immunization with autogenous vaccine and scarlet-fever streptococcal toxin.

"6. Comparable pseudomembranes were produced experimentally in rabbits with subconjunctival injections of Streptococcus haemolyticus and its toxins.

"7. When the inefficacy of ordinary therapeutic measures is contrasted with the results obtained in this case, it seems justifiable to recommend the use of scarlet-fever streptococcal antitoxin in cases of pseudomembranous conjunctivitis which are not due to readily recognizable causes."

W. S. REESE.

Comparative Ophthalmology

COLOR OF EYE IN DOMESTIC PIGEONS. R. LIENHART, Compt. rend. Soc. de biol. **121**: 1415, 1936.

The colors of the irises of pigeons are of importance in genetic studies. Nine types are distinguishable: (1) orange, (2) yellow, (3) brown, (4) white, (5) red-speckled, (6) red currant, (7) black, (8) asymmetrical and (9) heterochromic. The primitive and most typical iris, the orange, shows yellow coloration at the internal margin and red at the external margin. The other varieties are derivations of this type, the brown iris having in addition brown-black chromatophores over its vascular surface.

J. E. LEBENSOHN.

DISTRIBUTION OF VITAMIN C IN THE EYE OF THE RABBIT. B. NAKAMURA and O. NAKAMURA, Arch. f. Ophth. **135**: 87 (Jan.) 1936.

The eyes of fourteen white rabbits were enucleated, and each eye was divided into the following fractions: pupillary portion of the iris, ciliary portion of the iris, ciliary body, aqueous, cornea, retina and choroid, anterior half of the lens, posterior half of the lens, sclera and vitreous. The total vitamin C content of each of these fractions was determined and (apparently) expressed in milligrams per hundred grams fresh weight of the respective tissue. The average for the pupillary portion of the iris was relatively the greatest, viz., 50 mg.; those for the other fractions dropped in the aforementioned order from 28 to 8 mg. The significance of these figures is not clear.

P. C. KRONFELD.

Congenital Anomalies

TRUE CONGENITAL DISTICHIA. K. T. A. HALBERTSMA, Arch. d'opht. 52: 738 (Oct.) 1935.

A review of the literature on this rare condition shows that only about 50 cases have been reported. It appeared in 1 of 50,000 patients in Elschnig's clinic. In Vienna, in a clinic with a yearly attendance of 20,000 persons, only 3 or 4 cases had been seen in thirty years. According to the author, the definition given by Stellwag von Carion in 1858 remains the best. Study of these cases has shown that the aberrant lashes are always associated with modified meibomiam glands. For this reason treatment by epilation or electrolysis is of no avail. Halbertsma describes a case in which the condition was successfully treated by excision of a narrow strip of skin and mucous membrane including the aberrant lashes. Photomicrographs showing the cilium arising in a gland are presented. No other members in the family were similarly affected.

S. B. MARLOW.

POSTERIOR LENTICONUS AND FALSE LENTICONUS. ANTONIO ALCALÁ LÓPEZ, Arch. de oftal. hispano-am. 35: 505 (Oct.) 1935.

This is a report of a case of bilateral eccentric pseudolenticonus in which the optical and the clinical picture corresponded exactly to those described in previous reports of cases of posterior lenticonus, but in which an examination with the slit lamp showed a normal capsule and a normal position of the lenticular nucleus. After reference to the cases of Vogt, Riedl, Krasso and Jakobowicz, whose observations were confirmed by this method, and to the studies of Pergens, Bach, Beck, Hess and von Hippel, which show the nonexistence of lenticonus in eyes of rabbits and pigs clinically presenting the classic complex of symptoms, Alcalá López agrees with Dor in considering most reported cases of lenticonus as examples of pseudolenticonus.

He attributes the picture to a localized thickening of the lens with increase of its refractive index, possibly due to aberrant lenticular cells of an abnormal type, separated from the anterior epithelium during fetal life, which were preserved and which developed in the midst of the normal ones from the posterior epithelium, or to pathologic changes similar to the formation of refringent globules in flat cell epithelioma (cholesteatoma of Müller).

C. E. FINLAY.

Cornea and Sclera

KERATITIS OF NASAL ORIGIN. A. MAGITOT, H. TILLÉ and DUBOIS-POULSEN, Ann. d'ocul. 172: 1 (Jan.) 1936.

The nasal origin of certain diseases of the anterior segment of the eye is well recognized and is not now discussed any more than the origin of optic neuritis in a focus of infection in the nasal sinuses. Numerous cases are cited in detail, and conclusions are drawn regarding (1) phlyctenular keratoconjunctivitis of children and of adults,

(2) subepithelial keratoconjunctivitis of adults and (3) keratitis in the course of follicular conjunctivitis traceable to a nasal origin.

In the first type of keratoconjunctivis the nasal lesion seems to act by spread of the infection organisms, by its position and by its rôle as a focus of infection; in the second type, on the contrary, the nasal lesion acts by irritation and consequent disturbance of nerves. The third type appears to be made up of both the foregoing types, that is, the type due to action from a focus of infection and that due to nervous influences.

In the presence of clinical keratitis it is most important to examine the nose and treat all nasal malformations. In children removal of adenoids and hypertrophied tonsils assists in the cure. In adults shrinking the mucous membrane of the nose with cocaine can easily be done by the ophthalmologist and often gives an indication concerning the origin of the condition. Further treatment should be completed by the rhinologist. A routine nasal examination should be made in every patient suffering from a corneal disturbance. A bibliography accompanies this article.

S. H. McKee.

Choroidal Complications in Parenchymatous Keratitis. N. Colomba, Ann. di ottal. e clin. ocul. **64**: 1 (Jan.) 1936.

Colomba examined twenty-five patients who had recovered from interstitial keratitis with complete clearing of the cornea. The examination included ophthalmolscopy and study of the visual fields, the central vision and the peripheral vision, recorded by the method of Contino. In seventeen patients only one eye was affected, and seven of these showed no changes in the fundus of either eye. Three of the seven had normal results in functional tests, while four showed slight contraction of the fields and slight reduction in peripheral visual acuity. Of the ten others having only one eye affected, six showed small isolated foci of choroiditis peripherally in both fundi; most of the foci were without pigment, but some were surrounded by halos of it. Three showed these changes in the eye not affected by keratitis and larger yellowish-red spots, often confluent and covered with pigment, in the affected eye. One showed no changes in the fundus of the unaffected eye and large foci of choroiditis in the affected eye. Vision ranged from 9/10 to 10/10, with the changes in the fields and indirect vision corresponding to the changes in the fundus in most cases, while in some of the affected eyes such functional changes were noted in parts of the field not corresponding to the parts of the fundus showing changes.

Of the twelve patients in whom both eyes were affected, three showed no changes in the fundi. Three showed slight changes in both fundi. Two showed a combination of small and large foci of choroiditis in both eyes. Two showed only large areas of choroiditis in both eyes. Three showed only small foci in one eye and a combination of large and small foci in the other. All twelve patients had vision of 9/10 to 10/10 in both eyes but changes in fields and indirect vision which in some cases did not correspond with the fundus changes.

In the patients with monocular involvement most of the lesions appeared to be old, and when fresh lesions were seen these occurred

with about the same frequency in the eyes unaffected by keratitis. This is evidence that the choroiditis occurs without any direct relationship to the attack of keratitis, although it may occur during the attack.

In twenty-seven of the twenty-nine cases the condition was due to congenital syphilis.

The article includes a bibliography.

S. R. GIFFORD.

THE MOST RECENT CONTRIBUTIONS TO KERATOPLASTY EMPLOYING THE CORNEA OF THE CADAVER. V. P. FILATOV and L. P. SCHMOULIAN, Arch. di ottal. **43**: 57 (Jan.) 1936.

The results of keratoplasty in the Ophthalmologic Clinic of the Institute of Medicine of Odessa, U. S. S. R., are reviewed. Of forty-eight operations on eyes without grave complications such as staphyloma or buphthalmos, fourteen, or 29 per cent, were successful in that the graft remained transparent enough to permit useful vision. In every eye in which the operation was successful the cornea had retained some transparent portions before the operation, and in such eyes, which present the only really favorable conditions for keratoplasty, the percentage of successful grafts was 54. Illustrative cases in which the usual method was followed, that of employing the cornea of a living person, are described.

More recently a number of operations were undertaken with the corneas of persons dead from two to fifty-five hours. Blood from the heart was employed for the Wassermann or the Kahn test, and use was made only of material from patients whose blood was without a positive reaction and who showed no evidence of malignant growth, tuberculosis, diabetes or septicemia. The material was preserved in a clot of blood or in citrated blood in sealed dry bottles at from 4 to 6 C. until used. Thirty-five operations were performed. The results of twelve have been followed for longer than nine months. In six eyes the grafts have become opaque. In the other six more or less transparency has been retained, allowing vision of from 1/180 to 1/10. In one eye material from a cadaver preserved for thirty hours remains clear after eight months, with vision of 3/10. On the whole, material from the cadaver has shown no more tendency to become opaque than material from the living.

S. R. GIFFORD.

SUPERFICIAL KERATITIS AND VITAMIN A. F. STOCKER, Schweiz. med. Wchnschr. **66**: 335 (April 4) 1936.

In 1889 E. Fuchs described a condition in which the conjunctiva was moderately inflamed, following which small gray flecks appeared, often in groups, in the central part of the cornea, which he called keratitis punctata superficialis. Vogt studied the condition on the advent of the slit lamp but was unable to assign a cause for it. Some thought it might be related to herpes corneae simplex, while others felt that a physical agent, such as ultraviolet rays, or a chemical caused the disease. Related or similar lesions were given a "nervous" basis. Antiseptic salves seemed to help some patients, while others acquired permanent clouds in the cornea in spite of treatment. Finally evidence accumulated presenting the factor of some general derangement

of the bodily tissues as being the most important cause of superficial keratitis. Often infants with deficiency disease were found to have a like involvement of the corneas. Increase in the ingestion of vitamin A worked miraculous cures, as demonstrated in three cases cited by Stocker. Not only the local ocular condition was benefited, but the patient's general health was markedly bettered. Stocker recommends liver preparations with a daily dosage of from 8,000 to 16,000 units. Prompt healing of the corneal disease is constantly noted.

L. L. MAYER.

General Diseases

LIPODYSTROPHIA PROGRESSIVA WITH OCULAR COMPLICATIONS. J. W. CHARLES and M. H. POST, Am. J. Ophth. **19:** 126 (Feb.) 1936.

This condition occurred in a woman whose case was first reported in 1926 before the American Ophthalmological Society. In 1928, because of corneal ulcers she was admitted to Barnes Hospital in the hope of advancing the blind eye in the orbit and thereby bringing it in contact with the lids. A saline solution was injected into the orbit, which caused the globe to move forward ¼ inch (0.64 cm.). At a second operation the median palpebral ligament was cut, as was also the palpebral fascia close to the lacrimal sac for about ¼ inch above and below the ligament, and also the lateral palpebral ligament and almost ½ inch (1.27 cm.) of the attachment of the palpebral fascia above and below the ligament. There was improvement; the ulcer of the right cornea healed, and the left cornea cleared above and to the nasal side. Despite a tarsorrhaphy later, however, the patient ultimately became blind and in 1934 showed such extensive loss of fat about the head and neck that one could almost palpate the cervical processes from in front. The extremities were greatly emaciated, though there the loss of fat was not so marked. The hair had fallen out rather profusely, and the thyroid gland was distinctly larger. The condition is considered to be an abiotrophy.

W. S. REESE.

VASCULARIZATION OF IRIS AND CORNEA IN DIABETES. R. D. LAWRENCE and A. H. LEVY, Brit. J. Ophth. **20:** 198 (April) 1936.

Lawrence and Levy report vascularization of the iris and cornea in a 60 year old man with diabetic retinitis. In the right eye there were a few retinal hemorrhages, and in the left, gross hemorrhages around the disk and macula. Secondary glaucoma supervened in the left eye with hyphemia. Later, vessels developed in the posterior layers of the cornea and in the iris. In seven weeks the vessels in the cornea disappeared. Both eyes finally became blind. The right eye also became glaucomatous.

W. ZENTMAYER.

PAGET'S OSTEITIS DEFORMANS WITH BILATERAL OPTIC NERVE ATROPHY. M. VIDAUR, Arch. de oftal. hispano-am. **36:** 1 (Jan.) 1936.

A woman 75 years of age with typical lesions of osteitis deformans had also atrophy of both optic nerves. The vision was reduced to 1/8 and 1/10 in the right and the left eye, with concentric limitation of

the fields for white and colors. On macroscopic and roentgenographic examination typical lesions were found in the bones of the skull, thorax, pelvis and extremities, together with calcemia and calciuria.

Vidaur reviews at length the literature on Paget's, Recklinghausen's and allied bone diseases dependent on defective calcium metabolism and discusses their relations to parathyroid function. He also refers to ocular lesions reported in connection with such diseases, the majority being of a trophic nature (choroiditis, retinal hemorrhages, chorioretinitis, atrophy of the optic nerve, yellow spots in the macula and retinal periphery, diplopia, paralysis of the external rectus muscle, retinal exudation, sclerosis of retinal vessels and narrowing of the sphenoidal fissure and optic canal. He attributes the atrophy of the optic nerves in the case which he reports to circulatory disturbances, while most authors regard narrowing of the optic canal as the cause.

In connection with the treatment reference is made to the satisfactory results obtained by extirpation of parathyroid adenoma when this exists, with ligature of thyroid arteries and cauterization of the vascular network, and to the uselessness of these surgical measures and calcifying therapy when there is no adenoma, as in the reported case.

C. E. Finlay.

Glaucoma

On the Surgery of Glaucoma: Mode of Action of Cyclodialysis. O. Barkan, S. F. Boyle and S. Maisler, Am. J. Ophth. **19:** 21 (Jan.) 1936.

Heine's development of cyclodialysis is discussed, also the theory on which it is based. With the idea of determining the mode of action of cyclodialysis fourteen patients with primary glaucoma on whom cyclodialysis had been performed were examined by a technic to be published later. The following summary is given:

"Our gonioscopic investigations show that the establishment of communication between the anterior chamber and the suprachoroidea is the mechanical *sine qua non* in the successful action of cyclodialysis in cases of primary glaucoma observed by us. This is of evident surgical and clinical importance. In practice, the method has the added advantage of enabling us to determine the reason for lack of effect of the operation in a given case and of indicating when a repetition of the operation is necessary in order to establish the permanent dialysis which insures a successful result."

W. S. Reese.

The Etiology of Chronic Primary Glaucoma. E. O'G. Kirwan, Brit. J. Ophth. **20:** 321 (June) 1936.

Epidemic dropsy occurred in parts of India in 1934 and 1935, and during this period 1,695 persons with primary glaucoma came to the Eye Infirmary of the Medical College Hospital in Calcutta. Epidemic dropsy is the only disease known in which glaucoma forms an integral part, and hence it is the biggest clinical lead investigators have ever had to the pathogenesis of glaucoma; it places primary glucoma in its proper environment, namely, the symptom complex of a general disease.

The author's summary follows:

"In the sera of patients suffering from epidemic dropsy the relative viscosity and the surface tension are lowered below normal. The p_H remains unaltered while the buffer action is also below normal. The protein fractions show a considerable reduction in albumen while the globulins are found to be increased. The increase of pseudo-globulin is more marked than that of eu-globulin. In the aqueous humor of patients suffering from epidemic dropsy glaucoma, there is a marked increase of the albumins while the globulins remain the same. The normal ratio of albumen to glubulin is 0.44 to 1.0 whereas in the aqueous humor of epidemic dropsy glaucoma, the albumen is more than the globulin in the ratio of 2.3 albumen to 1.0 of globulin. In a certain number of patients suffering from epidemic dropsy glaucoma, a histamine-like body has been proved to be present in the aqueous humor. The whole uveal tract shows a marked dilatation of the capillaries, and there is no evidence of any inflammatory process."

The article is illustrated.

W. ZENTMAYER.

ENLARGEMENT OF THE NASAL PORTION OF THE VISUAL FIELD IN SEVERAL PATIENTS WITH CHRONIC GLAUCOMA AFTER SCLERO-IRIDECTOMY. G. OURGAUD, J. SÉDAN and A. ROUX, Ann. d'ocul. **173:** 353 (May) 1936.

The apprehension of the ophthalmologist who makes a fistula in an eye with chronic glaucoma in which the visual field runs into the point of fixation is well known. He fears further shrinking of the field even beyond the macula, causing the patient to lose central vision and in some cases all vision, to the subsequent indignation of the patient and the patient's family. The operation advocated by Lagrange insures normal ocular tone and the conservation of visual acuity, which in numbers of patients permits a return of better vision even though in these the contracted visual fields have not shown any improvement. Six illustrative cases are reported.

The writers stress the point that enlargement of the visual field is usually very slow, being hardly noticeable until after several years. The enlargements are not often seen, because only the discontented patients return; the satisfied ones with enlarged fields do not return. It is for this reason that statistics on this subject are not reliable. The authors believe that if one could see patients cured of glaucoma with a contracted field five or six years after operation one would also discover very often some with conditions analogous to those presented here, that is, with enlargement of the visual field.

S. H. MCKEE.

Injuries

INJURIES TO THE EYE CAUSED BY SPORTS. S. de GRÓSZ, Brit. J. Ophth. **20:** 148 (March) 1936.

This most interesting article does not lend itself to abstracting. The whole range of sports is considered, including automobiling. Protective measures are also discussed. De Grósz says that if one peruses the list of sport injuries described one will say that some of them are rare

contingencies, even curiosities, such as those that occur in angling and Sandow. Some of them, however, are typical occurrences with which one must reckon (boxing, skiing). Are they avoidable? Alas, only partially. The necessity for protection against excessive light in high altitudes has sunk into public knowledge. The number of infections incurred in closed swimming pools, including aural infections, can be reduced by stricter control of the water. He discusses in detail the manner of protection in skiing. There is one more way to diminish the number of accidents, i. e., by increasing sport discipline. This would reduce, for instance, the number of hunting accidents. And here belongs the problem of training for sport, also.

W. ZENTMAYER.

ACID AND ALKALI BURNS OF THE EYE. D. I. BEREZINSKAYA, Sovet. vestnik oftal. **8**: 319, 1936.

This is an experimental study of chemical burns of the eye. During thirty-five years (1900 to 1935) there were admitted to the hospital of Helmholtz 876 patients who suffered from ocular burns caused by chemical, thermic and explosive agents. Of these, 196 had acid and 229 alkali burns. On rabbits' eyes Berezinskaya experimented with 50 per cent solution of sulfuric acid and 20 per cent solution of sodium hydroxide, but the destruction of the eyes followed too rapidly. She therefore used 30 per cent solution of sulfuric acid, 18 per cent solution of hydrochloric acid and 5 per cent solution of sodium hydroxide; these concentrations are met with more frequently in industrial and chemical hazards.

In the first series of experiments (on seven eyes of four rabbits) a study was made of the rapidity of the penetration of alkali and acids into the anterior chamber and vitreous. Sodium hydroxide was observed in the anterior chamber within five minutes after its instillation into the conjunctival sac. This alkali was found in the secondary aqueous within thirty minutes and within twenty-four hours. No alkali was observed in the vitreous at any time. Sulfuric acid did not enter the anterior chamber or the vitreous in five minutes, ten minutes or three hours.

In the second series seven eyes were burned with acids and seven with alkali. The clinical picture was studied with focal illumination and with the slit lamp. The eyes were enucleated at from four hours to twenty-two days after the burn and studied histologically. Detailed protocols of the experiments, five photomicrographs and two tables are given which illustrate the subject well. Some histories of patients in the hospital who had suffered burns with alkali and acids are given for comparison.

Berezinskaya comes to the following conclusions: 1. Alkali (5 per cent sodium hydroxide) penetrates the anterior chamber within five minutes. 2. Acid (30 per cent sulfuric acid) does not penetrate the anterior chamber. 3. Alkali and acid burns differ histologically. 4. The difference is noticeable in the first few hours, which explains the difference in the penetrability of the cornea for acids and alkali. 5. The pathologic process in alkali burns is diffuse. It affects all parts of the cornea except Descemet's membrane. The uveal tract is involved. The lens remains intact. 6. The process in acid burns is limited, super-

ficial. Secondary infection aids the spreading of the process into the deep layers with defect of tissue and formation of crusts. The lens becomes cataractous. The uveal tract is not always involved. 7. Descemet's membrane is very stable to both alkali and acids. 8. Characteristic of hydrochloric acid burns are the homogeneity of the corneal tissue and crust formation on the surface. 9. Acid burns frequently cause cataracts. 10. Clinically and histologically alkali burns are more severe than acid burns.

O. SITCHEVSKA.

Lacrimal Apparatus

DACRYOSTENOSIS IN CHILDREN. R. O. RISER, Am. J. Ophth. **18:** 1116 (Dec.) 1935.

Riser's conclusions are as follows:

"1. It was necessary to wait 3.5 months before satisfactory results were obtained in the most persistent of the congenital cases under conservative treatment, while the average time required for recovery was 1.4 months. Therefore, it would be well to wait for three or four months before probing, if the case is under control, for in two thirds of the cases of congenital dacryostenosis treated by expectancy plus antiseptic solution and pressure over the sac, we have seen the duct open without further interference.

"2. Probing, when necessary, can safely be performed satisfactorily with a number-two Bowman's probe without a canaliculotomy. The results with this simple procedure were uniformly satisfactory, and we see no reason for using larger probes in infants when conservative medical care plus conservative probing was effective in 97 per cent of our cases of congenital dacryostenosis.

"3. Only 50 per cent of our cases of acquired dacryostenosis were arrested by conservative and simple therapy. The other half have required or do require a dacryocystectomy or other major operation of the lacrimal drainage apparatus, thus showing a marked difference in comparison with the benign course of the great majority of congenital cases of dacryostenosis."

W. S. REESE.

DACRYOCISTORHINOSTOMY. J. BASTERRA, Arch. de oftal. hispano-am. **36:** 208 (April) 1936.

Basterra refers to the development of the operation since Toti described it and mentions Ohms', Dupuy-Dutemps' and his own contributions. He stresses the necessity of uniting by catgut suture the mucous membranes of the nasal fossa and lacrimal sac. He employs a single C-shaped flap with an anterior pedicle, recommends the opening of the bony canal by means of small trephines with avoidance of injury to the pituitary mucous membrane and resects the posterior margin of the sac incision. He also gives importance to prior roentgenographic examination of the sac after injection of barium sulfate or iodized poppy-seed oil 40 per cent, and to a preliminary rhinoscopic examination.

C. E. FINLAY.

Lens

POSTOPERATIVE DEFORMATION AND DECENTRATION OF THE PUPIL IN CAPSULAR CATARACT EXTRACTION. A. J. MANES, Arch. de oftal. de Buenos Aires **10:** 579 (Aug.) 1935.

Manes calls attention to the pyriform deformation and upward dislocation of the pupil independent of any loss of vitreous, iris inclusion in or adhesion to the operative wound seen at times after capsular extractions. He finds no pathologic explanation for it, not accepting Basterra's adhesion of vitreous to the iris or to the wound. He recommends the following prophylactic measures: correct corneal incision, reduction of the operative trauma to a minimum, spontaneous replacement of the iris by simple massage, thereby avoiding the introduction of the spatula or other instrument into the eye, and a small peripheric iridectomy.

C. E. FINLAY.

TRAUMATIC DETACHMENT OF THE LAMELLA OF THE CAPSULE OF THE LENS DURING IRIDECTOMY: REPORT OF TWO CASES. W. ROHRSCHNEIDER, Klin. Monatsbl. f. Augenh. **96:** 31 (Jan.) 1936.

Rohrschneider discusses and briefly describes the two types of detachment of a lamella from the anterior capsule of the lens: the senile and that caused by exposure to fire. After quoting publications in point he adds his observations on apparently a third type. Two women aged 51 and 74 had iridectomy for secondary glaucoma following iritis. Directly after operation each patient was found to have shreds of a lamella of the capsule of the lens in the anterior chamber. A lesion due to radiation could be ruled out. The shreds resembled fine glassy membranes. No defects could be detected on the anterior capsule of the lens with the slit lamp. These two cases and those cited from the literature show that such detachments do not result only from thermic lesions in furnace workers. They may result after chronic iritis of long duration, although it may be difficult to prove the presence of this disease. Topolanski and Elschnig found detachment of capsular lamellae histologically. An iridectomy, as in Rohrschneider's cases, or shrinking in the eyeball, as described by Elschnig, may lead to detachment of a lamella from the capsule of the lens.

K. L. STOLL.

EXPULSIVE HEMORRHAGE. M. I. AVERBACH, Sovet. vestnik oftal. **8:** 652, 1936.

Averbach advocates prophylactic trephining of the sclera on the second eye in cases in which expulsive hemorrhage has occurred in the first eye after extraction of a cataract. This method was applied previously by Verhoeff and Filatov on eyes in which expulsive hemorrhage was threatened, on the basis that the accumulated blood in the suprachoroidal space would flow through the artificial opening in the sclera instead of through the healed wound.

In three cases Averbach performed trephining near the equator with a 2 mm. trephine, and no expulsive hemorrhage occurred in the second eye.

O. SITCHEVSKA.

Lids

CHALAZION-LIPOGRANULOMATOSIS. A. HAGEDOORN, Am. J. Ophth. **18:** 424 (May) 1935.

Hagedoorn concludes that chalazion belongs to the large group of lipogranulomatoses. An inflammation induced by various organisms or by a simple occlusion of the ducts may be primary or, perhaps, due to nervous influences and certain general infections. W. S. REESE.

A CASE OF SECONDARY HAEMORRHAGE FOLLOWING CURETTAGE OF A MEIBOMIAN CYST. J. G. D. CURRIE and J. P. F. LLOYD, Brit. J. Ophth. **20:** 162 (March) 1936.

A woman aged 23 had had a cyst in the right lower eyelid and now presented 9 meibomian cysts distributed over the four eyelids. The cysts were all curetted under general anesthesia. Four days later a secondary hemorrhage of alarming nature occurred at the site of the cyst which had been curetted once before. A 000 silk suture was passed twice right through the thickness of the lid just to the basal side of the cyst and tied over a rubber tube laid on the skin surface. Forty-eight hours later a second profuse hemorrhage occurred, requiring a suture to be passed around the cyst. The patient had been suffering from whooping cough for a few days. The coagulation and the bleeding time were normal. W. ZENTMAYER.

Methods of Examination

A VISUAL ACUITY TEST FOR MALINGERERS. J. N. DUGGAN, Brit. J. Ophth. **20:** 175 (March) 1936.

The test has been devised for the detection of malingering in illiterate persons and to determine the percentage of their loss of vision. The apparatus consists of an internally illuminated box, the face of which is divided into four equal rectangles, two of which contain green glass, one red and one white. In front of this box is placed one of a series of metal plates in which are apertures so arranged that by varying the way in which the plate is placed before the colored squares as many as four different variations of the position of the apertures are possible. The apertures are in Snellen sizes of 6/24 to 6/6. As many as twenty-one variations can be quickly made. Accurate guessing on the part of the patient is thus rendered impossible. W. ZENTMAYER.

INTENSITY OF LIGHT IN RELATION TO THE EXAMINATION OF THE EYES. C. E. FERREE and G. RAND, Brit. J. Ophth. **20:** 331 (June) 1936.

Ferree and Rand deal with the question of the intensity of light in relation to the correction of errors of refraction, the standard rating of acuity and its rating for other purposes, the determination of the near point of vision and the apparent range of accommodation, and the study of the visual field with the tangent screen and the perimeter.

The article does not lend itself to abstracting. It contains a bibliography. W. ZENTMAYER.

Neurology

AN ELECTROMYOGRAPHIC STUDY OF MYOTONIA. D. LINDSLEY and E. CURNEN, Arch. Neurol. & Psychiat. **35**: 253 (Feb.) 1936.

The authors present two cases of myotonia. The chief symptom of this condition is persistent contraction of a muscle after voluntary, mechanical, electrical or, in some instances, reflex stimulation. In the first case the extrinsic muscles of the eye were involved, but no details of the involvement are given. In the second case there was slight ptosis of both lids, also slight internal strabismus of the right eye.

The cases are interesting examples of involvement of the extrinsic ocular muscles in a general skeletal muscular disease.

R. IRVINE.

A CLINICAL AND ELECTRICAL STUDY OF HEREDITARY AND FAMILIAL PARTIAL FACIAL DIPLEGIA. R. HUMBERT and R. ROSSANO, Ann. d'ocul. **173**: 369 (May) 1936.

Facial diplegia of cortical origin is a syndrome well known in France, particularly since the work of Charles Foix and his pupils. It has interested ophthalmolgists from more than one point of view. As the name indicates, it affects not only the muscles of the face, particularly the orbicularis muscles of the eyelids, but frequently the oculomotor muscles, so that there are disturbances of sight.

Acquired facial diplegia of peripheral origin begins as a lesion of the peripheral neuron of the facial nerve, first on one side and then on the other. One would think that this condition was exceptional, but it has been noted by several authors. The cases are extremely rare. Recently, Alajouanine, Huc and Gopcévitch have reported the occurrence in four children of a congenital syndrome characterized by clubfoot, facial paralysis and paralysis of the sixth nerve, all bilateral. Humbert and Rossano have recently observed in a young man who wished to be operated on for bilateral ptosis an incomplete facial diplegia, which he asserted was not only congenital but also familial and hereditary.

The details of the case, two diagrams and a bibliography are given.

S. H. MCKEE.

Ocular Muscles

THE MARCUS GUNN PHENOMENON: REPORT OF A CASE WITH SUGGESTIONS AS TO RELIEF. F. GRANT, Arch. Neurol. & Psychiat. **35**: 487 (March) 1936.

A case of the Marcus Gunn phenomenon is described in which movement of the lower jaw to the left caused synchronous elevation of the right upper eyelid. With the face at rest there was moderate ptosis of that eyelid; it could not be raised voluntarily as far as the left. There was right enophthalmos of 1 mm., and the right pupil showed slight miosis as compared with the left. Both pupils reacted promptly to light and in accommodation. A ciliospinal reflex could not be elicited in the right eye but was active in the left.

Movement of the jaw to the left with the mouth open or closed, whether performed slowly or rapidly, was promptly followed by upward movement of the right eyelid until 3 mm. of sclera was visible. No other movement of the jaw produced this effect. It was noted accidentally that after instillation of 1 per cent homatropine hydrochloride, the movement of the jaw to the left no longer produced elevation of the right eyelid.

In the literature Grant was able to find reports of 100 cases of this phenomenon with slight variations. He reviews briefly those having a bearing on the case under discussion. This case is the only one reported in which the effect of homatropine on the condition was recorded and the only one in which there was surgical intervention. The motor supply of the right external pterygoid muscle was sectioned to prevent movement of the jaw to the left. In this way the associated elevation of the right eyelid, which had occurred particularly during movements of mastication, was prevented. The slight enophthalmos and miosis on the right were no longer obvious. Various interpretations of the observations are given, none of which seem to the author entirely adequate.

R. IRVINE.

THE PRINCIPLES OF ORTHOPTIC TRAINING. S. MAYOU, Brit. J. Ophth. **20:** 360 (June) 1936.

This is an elementary treatise on orthoptic training, covering the principles and methods involved. It does not lend itself to abstracting.

W. ZENTMAYER.

Operations

SCLERAL INSERTION OF SPHERE AND SOLID OVOID. A. POULARD, Ann. d'ocul. **173:** 120 (Feb.) 1936.

When Poulard first began to practice insertion of the solid sphere in May 1917 he preserved the greatest possible amount of fibrous tissue in order that the sphere might be better enveloped. Since then he has employed smaller spheres, not because of failure or operative difficulties but because of great improvement in the manufacturer's art. The simple shell artificial eye may now be replaced by a glass one of double shell (the reform eye).

The subject is divided into operative technic (first stage, disinsertion of the conjunctiva; second, removal of the anterior segment; third, enucleation; fourth, putting the ovoid in place and suturing), postoperative pain and serous infiltration, results, indications and complications. There are six illustrations.

S. H. MCKEE.

EPITHELIAL INLAY FOR THE ENLARGEMENT OF THE CONJUNCTIVAL SAC FOR AN ARTIFICIAL EYE. J. F. S. ESSER, Ann. d'ocul. **173:** 208, 1936.

After enucleation it is often difficult and sometimes impossible to conserve the conjunctival sac so that an artificial eye may be worn

satisfactorily. In all cases it is possible by means of an epithelial inlay to form a sac of the dimensions required. Esser introduced this method in 1916, and it has been accepted and used by many surgeons in different parts of the world, especially by those who have been doing repair work among victims of the war. Esser describes the operation in detail. The article is illustrated with five photographs.

S. H. McKee.

Several Operative Technics. De Saint Martin, Ann. d'ocul. **173:** 292 (April) 1936.

De Saint Martin holds that it is not without interest to review certain operative procedures practiced in France, especially those which enjoy a well merited favor among foreigners. It also seems useful to him to describe certain technics relative to the surgery of strabismus and of the eyelids, which he saw at Budapest. They were precise and simple. He then gives details of the procedures of Professor de Grósz and Professor Blaskovics. Seven drawings illustrate the article.

S. H. McKee.

Orbit, Eyeball and Accessory Sinuses

Exophthalmos of Basedow's Origin. C. Weskamp and C. Alvarez, Ann. d'ocul. **173:** 273 (April) 1935.

Exophthalmic goiter frequently shows itself first by ocular symptoms, and for this reason oculists are very often the first to be consulted. It is usually not difficult to find other symptoms which the patient has not noticed, as they appear later in the course of the disease. In the cases recorded here, on the contrary, exophthalmos appeared without any of the other ordinary signs of Basedow's disease, but the exophthalmos nevertheless had the characteristics of Basedow's disease. In most of the cases it was unilateral, reducible, without pupillary alterations and without paralysis of the extrinsic muscles. Retraction of the upper eyelid and asynergy of ocular movements were frequently seen.

Nine cases are published in detail, with a series of photographs.

S. H. McKee.

Pseudotumor of the Orbit. M. Soria, Arch. de oftal. hispano-am. **36:** 310 (June) 1936.

Soria reports a case of pseudotumor of the orbit. Biopsy showed lymphocytic infiltration of the cellular tissue. Etiologic investigation yielded a negative Wassermann reaction, normal roentgen dental observations and a positive Mantoux reaction. Roentgen examination of the chest showed calcified nodules in the lung and calcified lymph glands at the pulmonary hylus. Treatment with methylic antigen resulted in a complete cure.

C. E. Finlay.

Physiology

CONGENITAL AND ACQUIRED DEFICIENCIES OF FUSION. A. BIELSCHOWSKY, Am. J. Ophth. **18:** 925 (Oct.) 1935.

This paper does not lend itself to abstracting. Bielschowsky discusses fusion and cites a case of horror fusionis in which considerable experimentation was done, the patient being operated on several times. Fusion was not obtained until the proper aniseikonic correction was found; then the patient obtained binocular single vision in the whole field of fixation encompassed by his glasses and for the first time achieved depth perception.

W. S. REESE.

RESEARCH ON THE BLOOD PRESSURE IN THE CENTRAL RETINAL ARTERY. S. SUGANUMA, Klin. Monatsbl. f. Augenh. **96:** 74 (Jan.) 1936.

Suganuma and Uyemura in a previous paper reported on a new method of measuring the blood pressure in the retina. For this they used an ophthalmodynamometer of their own device. Suganuma now publishes his observations on the blood pressure in the central retinal artery in healthy persons and its relation to the general blood pressure. The researches of Bailliart, Bliedung and other authors are discussed, and Baurmann's view is accepted to the effect that the pressure in the large arteries of the body is hardly lower than that in the aorta, so that the blood is distributed to the divers organs under practically the same pressure, no matter how far they may be from the heart. Furthermore, basing his reasoning on Schultén's research on rabbit's eyes, he evaluates his own research thus: The pressure in the ophthalmic artery is certainly not lower than that in the larger arteries of the body. His results are described in detail and illustrated by two tables, one containing the data on the retinal arterial and the general pressure of sixty-five patients, the other those on the relation of the arterial retinal pressure of the one eye to that of the other, which may vary under normal conditions.

The central arterial pressure averaged 59.7 mm. of mercury in the systolic and 38.5 mm. in the diastolic phase, while the general systolic pressure averaged 120.4 mm. The relation of the arterial retinal to the general blood pressure was from 44×100 to 55×100. This shows a close relation between these two pressures. The pressure in the central retinal artery rises with age as the general blood pressure does. No relation exists between normal intra-ocular pressure and the blood pressure in the central retinal artery.

K. L. STOLL.

Refraction and Accommodation

VOLUNTARY CONTROL OF ACCOMMODATION. W. ZENTMAYER, Am. J. Ophth. **18:** 1134 (Dec.) 1935.

Zentmayer has observed two patients who could voluntarily use or relax their accommodation while looking at a distant object. In the first patient the change in the curvature of the lens accompanying this

"accommodation" could be seen, and there also appeared during this act an esophoria of about 15 degrees. He makes the following comments:

"In the first case there is apparently a tendency to spasm of accommodation in infinity accompanied by excessive convergence, though the possibility of the reverse sequence cannot be entirely excluded; that is, that the primary anomaly is a convergence excess accompanied by excessive innervation of accommodation.

"In the second case there is a subnormal accommodation impulse as well as a controlled accommodation. The existence of a high exophoria for near with the refraction error is due to lack of innervation of the interni as a result of the relaxation of accommodation. The esotropia present without correction of the hyperopia is the ordinary accommodation squint.

"In both cases the patients were advised to have a thorough physical examination, with special attention to the teeth because of the possibility of reflex disturbance.

"If apparent discrepancies are noted in the details of these cases it should be remembered that we were dealing with a physical function which is necessarily variable, and as the tests were in part subjective it was difficult for the examiner to exercise a control."

W. S. Reese.

Acquired Progressive Myopia of 20 Diopters: Report of a Case. B. Kayser, Klin. Monatsbl. f. Augenh. **96**: 369 (March) 1936.

A man aged 36 had never noted any ocular disturbances, not even after he was shot through the head in 1917. Some time after the war, while perfectly well, he noticed a decrease of his vision, and in 1929 he therefore applied for an invalid's rent. His myopia amounted to 11 diopters at that time, and black foci with minute retinal hemorrhages were observed in the macula lutea of each eye. Recently the myopia had been 20 diopters with an astigmatism of 2 diopters, and the vision was reduced to the counting of fingers at 4 meters. The outlines of the fields of vision were normal, but in each eye a large central scotoma existed for white and colors. Large white foci developed subsequent to 1929 in the centers of the fundi around the disks and maculae. A large black pigmented focus was present in each macula. Kayser thinks that severe pathologic processes, associated with hemorrhages, softened the posterior walls of the eyeballs so that gradually ectasia was formed by force of the intra-ocular pressure. A similar case, published by Fleischer in 1905, is cited.

K. L. Stoll.

Retina and Optic Nerve

The True Conception of the Operative Cure of Detachment of the Retina: The Closure of the Tear or the Drainage and Adhesions Produced. C. Pascheff, Arch. d'opht. **52**: 717 (Oct.) 1935.

Pascheff has on several previous occasions maintained that retinal tears are not the cause of retinal detachment but are secondary degen-

erative changes. Nature cures detachment by resorption of the subretinal fluid and by scar formation, i. e., chorioretinal adhesions. He describes an operation which aids nature. The procedure consists of exposing the sclera in the area of the detachment without bothering especially about localizing the tear. The choroid is then exposed by trephining the sclera on either side of a rectus muscle with a 1.5 mm. trephine. The choroid is then punctured with a diathermic needle to allow the subretinal fluid to escape and for electrocoagulation of the choroid, creating two fistulas. The conjunctiva is then sutured. Two detachments successfully treated are described. On the basis of many similar successes by this method Pascheff concludes not only that a tear is not the sine qua non of detachment but also that its closure is not the sine qua non of its cure. The most important considerations are the evacuation of the subretinal fluid and the production of adhesions.

S. B. MARLOW.

THE COMPARATIVE VALUE OF DIFFERENT TECHNICS FOR CLOSING RETINAL TEARS. P. VEIL and M. A. DOLLFUS, Arch. d'opht. **52**: 781 (Nov.) 1935.

Veil and Dollfus review five years' experience with various operative technics in three hundred cases of detachment of the retina. The percentages of lasting cures obtained with the various procedures were as follows:

Obliterating thermopuncture (the oldest cure almost five years)	49
Suprachoroidal galvanocauterization	58
Juxtachoroidal galvanocauterization	62
Chemical technic (Guist)	33
Perforating diathermic coagulation	55
Pyrometric diathermic coagulation (Coppez)	58

These averages would be above 70 per cent if only recent favorable results were considered. Recurrences in 10 per cent were observed for all methods.

The authors favor juxtachoroidal galvanocauterization because it is simple and can be controlled ophthalmoscopically. The adhesions produced form rapidly and shorten the length of time the patient has to be kept in bed. They have given up Guist's operation. The difficulties of instrumentation they feel are disadvantages for all the methods of diathermy, although good results are produced. No matter what procedure is used, provided obliteration, seclusion or exclusion of the tears is accomplished, the results are the same.

S. B. MARLOW.

REFLECTIONS ON THE PATHOGENESIS OF DETACHMENT OF THE RETINA. R. RUBBRECHT, Arch. d'opht. **52**: 786 (Nov.) 1935.

Because there are many points still unsettled, Rubbrecht in this report discusses some of the problems in connection with the pathogenesis of detachment of the retina. He is in accord with Gallois in the suggestion that some constitutional factor underlies the local cause of detachment. A tear of the retina is not essential to a detachment.

He presents some very interesting observations that tend to support this contention. One was the early observation of a case in which no tear was found. The condition subsided after the patient remained in bed for a time, reappeared when he got up and disappeared when he was put to bed again. The chief argument in favor of a tear as essential has been the success with which operative closure of the tear effects a cure. Rubbrecht points out that many detachments with which no tears were found have been reported as cured. He does not believe it necessary to infer that a tear is present in an unreachable portion of the retina. He cites a case in which a tear was seen to be closed by thermopuncture but in which the detachment persisted. He cites a second case in which a suture as used by himself cut a linear hole in the retina, aggravating the detachment, which later healed. The question of adhesive bands between the vitreous and the retina which pull the retina away is also considered. The point is made that all forms of treatment used at the present time tend to produce such bands. All these considerations lead him to believe that the local cause of detachment lies in the failure of the mechanism that naturally maintains the retina in place, as has been suggested by Rollet. As a result of these considerations he concludes that the most important function of any method of treatment is to produce artificial adherence of the retina at the place where the natural adherence fails. How this is done is relatively unimportant. Closure of the tears he does not believe to be essential.

S. B. MARLOW.

DIFFERENCES OF THE LEVEL OF THE CENTRAL RETINAL VESSELS. C. WESKAMP, Klin. Monatsbl. f. Augenh. **94:** 506 (April) 1935.

Examinations of the caliber, structure and course of the central retinal vessels were hitherto made in the frontal plane only. Weskamp explains why these vessels cannot constantly remain in the same plane when the intravascular pressure and the intra-ocular tension change. He bases his observations on the fact that the intraneural portions of the central vessels run in the axis of the optic nerve and that the vessels form an obtuse angle on entering the eyeball. This angle becomes more obtuse as soon as the intra-ocular tension decreases while the blood pressure remains the same, and vice versa. The changes of the angle depend on the intravascular pressure if the intra-ocular tension remains unchanged. The difference of pressure in the arteries and veins results in a difference between the angles formed by arteries and veins: the arterial and venous angles. The measurements were taken with Thorner's large ophthalmoscope. A number of tables illustrate the detailed description of this research on thirty persons of both sexes and varying ages, with normal physical findings. The artery lay higher than the vein in fifteen persons, lower in thirteen and in the same plane in two persons. The difference in level amounted to between 0.05 and 0.29 mm.

Some patients with cardiorenal disease and all those with hypertension showed simultaneous variations of the arterial pressure and the level of the blood vessels. The significance of the differences of level in the central retinal blood vessels in the course of diseases has not yet been found.

K. L. STOLL.

ANGIOMATOSIS OF THE RETINA (VON HIPPEL-LINDAU): REPORT OF A CASE. O. KARASEK, Klin. Monatsbl. f. Augenh. **95:** 163 (Aug.) 1935.

Karasek reports a case of angiomatosis of the retina in a man aged 27. The patient's mother lost one eye as a result of glaucoma and had only 15 per cent of the normal vision in her other eye owing to the same ocular disease. Her mother was blind from an unknown cause. The eyes of the patient's brother and his two sisters and their seven living children were normal; his father died from a pulmonary abscess. The patient, during his school years, suffered from headaches on arising; when he was about 19, pain in the region of the right kidney developed and parietal headache occurred especially on coming or going from a warm room to the cold outside. Two years later, attacks of vertigo lasting for a few seconds set in, and soon afterward a spot was noticed in front of the right eye; a second spot was noticed in the upper nasal field, associated since 1933 with a positive central scotoma and failing vision. The anterior sector of the right eye was normal. Extremely fine dustlike and filiform opacities were observed in the vitreous. A colored picture of the fundus shows hyperemia of the disk, an enlargement of the upper temporal retinal vein to four times the normal size and a distention of the upper nasal artery to twice the normal width. Both led nearly straight upward into a tumor which was located about 8 disk diameters above the disk. The tumor protruded into the vitreous to a height of about 5 diopters, and a capillary venous conglomeration showed near it. The retina around the disk was slightly detached. Numerous white dots were present in the macula, and others formed several clusters arranged in a semicircle about 3 disk diameters off from the disk. This arrangement resembled that of circinate retinitis. The left eye was normal.

This patient's eyes presented, according to Brand's division, the second stage of retinal angiomatosis (von Hippel), whereas the eyes of the grandmother presented the third stage and the enucleated eye of the mother probably the fourth.

The hereditary theory, accepted by many authors, appears to be supported by these observations.

There were slight neurologic symptoms, but these allowed no conclusion relative to the presence of an angiomatous cyst in the cerebellum.

K. L. STOLL.

HEREDITARY CONGENITAL ATROPHY OF THE OPTIC NERVE: REPORT OF A GENEALOGY. F. RIEDL, Klin. Monatsbl. f. Augenh. **95:** 332 (Sept.) 1935.

Riedl reports on hereditary atrophy of the optic nerve after Leber. The genealogy of a family in which this disease was observed in three generations is given in detail and the literature quoted. A short synopsis of sixteen genealogies reported by divers authors is added. Atrophy of the optic nerve had been present apparently since birth. The clinical picture was typical except for the irregularity of some defects of the field of vision. Roentgenograms of the area of the sella turcica did

not reveal any changes in the hypophysis. No general pathologic symptoms were present. The intermarriages in this family were not considered in concluding that hereditary congenital atrophy of the optic nerve is inherited according to the dominant type. K. L. STOLL.

Trachoma

THE CYTOLOGY OF TRACHOMATOUS AND FOLLICULAR CONJUNCTIVITIS. J. M. MARCUS and K. G. WAINER, Rev. internat. du trachome **13:** 68 (April) 1936.

Cytologic analysis offers valuable aid in the differential diagnosis of trachomatous and follicular conjunctivitis. Especially characteristic of trachoma are: (*a*) embryonal forms of lymphocytes, showing vacuolated protoplasm and nuclear mitosis; (*b*) the shadow cells of Humprecht, which result from cytolysis of these elements; (*c*) epithelial cells with degenerative alterations of the protoplasm, affecting mostly the nucleus. In follicular conjunctivitis, on the other hand, embryonal cells are absent, histiocytes are rare, epithelial cells are normal, and eosinophils are common. J. E. LEBENSOHN.

TRACHOMA IN PALESTINE. A. J. BRUCK, Rev. internat. du trachome **13:** 98 (April) 1936.

Because of the extensive prevalence of trachoma among the Arabs Palestine leads in blindness due to this disease. Visual impairment generally follows a secondary virulent infection with the Koch-Weeks bacillus. The modern Jewish immigrants are comparatively little affected, but their coreligionists, the Sephardim (descendants of refugees from the Inquisition), are in lamentable condition. The trachoma of Palestine is generally contracted in childhood (in 75 per cent of the cases, before the age of 3), and progresses rapidly, many of the school children showing complete cicatrization. J. E. LEBENSOHN.

Tumors

CONJUNCTIVAL PLASMOMA. J. PALLARÉS LLUESMA, Arch. de oftal. hispano-am. **36:** 61 (Feb.) 1936.

Conjunctival plasmoma in four persons is reported, with the clinical findings and pathologic observations. The four patients had trachoma; one, in the active stage, and the three others, in the cicatricial stage. The author reviews the literature on the subject. The statistics of the provincial hospital of Valencia show that the condition has been observed in 0.063 per cent of the total number of patients and in 0.4 per cent of those with trachoma. It generally occurs in connection with trachoma in the cicatricial stage. The tarsus is not as a rule involved except for hyaline or amylaceous degeneration. The process usually takes the form of papillomatous excrescences or crests situated on the margins of the superior tarsal conjunctiva and on the fornix and occasionally that of a sessile or polypoid growth; when it is located in the cornea this is usually smooth and turgescent. The disease is unaccompanied by pain or

spontaneous bleeding. It must be differentiated from aleukemic lymphatic hyerplasia, lymphocellular leukemic sanguineous hyperplasia, local lymphocellular hyperplasia and chronic diffuse lymphadenoid conjunctivitis. The microscopic lesion is a tumor-like plasmocytic infiltration with local hyperplasia and hyaline and amylaceous degeneration with occasional hyaline spheres (Russell's bodies). In connection with the pathogenesis of the lesion the author discusses at length the different views (some consider it as a neoplastic and some as an inflammatory lesion) and its relation to trachoma, and while he does not arrive at a conclusion he seems inclined to consider it, with trachoma, as a disease of the reticulo-endothelial system of the conjunctiva, characterized by an infiltration of reticular elements with follicle formation, defined by Löhlein and Pascheff as a "tumorlike formation with a plasmocellular hyperplasia." He advises surgical excision with roentgen therapy in cases of relapse.

C. E. FINLAY.

CONTINUATION OF STATISTICS ON UVEAL SARCOMA. E. VON HIPPEL, Arch. f. Ophth. **135:** 67 (Jan.) 1936.

This is a further report concerning von Hippel's series of 118 cases of uveal sarcoma (reported before the German Ophthalmological Society in Jena in 1922; *Arch. f. Ophth.* **129:** 552, 1933). Of the original 118 patients, 38 are still alive. Sixty-two per cent of the whole series have lived at least five years and 30 per cent ten years since enucleation of the sarcomatous eye. Only two thirds of the metastases occurred during the first five years; for this reason von Hippel objects to pronouncing a patient with uveal sarcoma cured because no metastasis or recurrence has developed during the first five years. He recommends a ten year limit, because after this period has elapsed metastases are "very isolated." If the ten year limit is adopted it will demonstrate that uveal sarcoma can be cured in only approximately 30 per cent of the cases. The following tabulation may be of interest:

Stage of Sarcoma at Time of Enucleation	Cases	Metastases	Deaths from Causes Other Than Metastases	Patients Alive at Time of This Report
I.....	61	23	14	24
II.....	48	25	10	13
III.....	9	8	..	1

P. C. KRONFELD.

ANGIOMA OF THE CHOROID WITH NAEVUS FLAMMEUS OF THE TEMPLE: REPORT OF A CASE. A. LUDWIG, Klin. Monatsbl. f. Augenh. **95:** 168 (Aug.) 1935.

In 1931, Lindenmeyer compiled a list of six cases of angioma of the choroid. In five of these cases the eyes were enucleated as presenting sarcoma of the choroid. In three other cases the symptoms pointed strongly toward the same disease, but histologic examinations could not be made as yet. In the remaining thirty-eight cases reported to date choroidal angioma was found incidentally in histologic examination; the eyes had been enucleated for absolute glaucoma.

Ludwig's patient, a woman aged 28, was born with a hemangioma of the temple the size of a pea. In the course of time it grew to the

size of a child's hand. The patient had no discomfort until headache set in two years prior to examination. Soon afterward the nevus assumed a darker hue, and vision failed in the left eye; temporal from the disk was a depigmented area of the retina, about 1.5 disk diameters in width. It showed a pigmented margin resembling the demarcation which occurs after a reattachment of the retina. In this case the retina was slightly detached, and the macular area was normal. Small yellowish-white and strongly refracting "foam bubbles" were observed in the retina. In Ludwig's opinion, they may have been akin to the vacuoles in the inner granulated layer described by Reiss. The grayish-blue color of the detached portion of the retina prompted him to interpret the lesion as an angioma. He considers this diagnosis corroborated by the presence of the facial nevus, the youthful age of the patient and the typical aspect of the demarcated area. According to Ludwig, the absence of degeneration of the macula and of a sector-shaped deficiency in the visual field, described by other authors, is to be explained by the peripheral location of the hemangioma.

K. L. STOLL.

Uvea

UVEOPAROTID TUBERCULOSIS: REPORT OF TWO CASES. I. D. KRUSKAL and J. M. LEVITT, Am. J. Ophth. **18:** 735 (Aug.) 1935.

Kruskal and Levitt give the following summary: "The salient features of the syndrome known as uveoparotid fever or uveoparotid tuberculosis are reviewed. The principal evidence supporting the belief that the condition is due to tuberculosis is presented. Two typical cases are reported. In the first case tuberculous infection was proved by biopsy of an enlarged lymph node which showed a tuberculous lymphadenitis."

W. S. REESE.

GREEN SPOT IN THE OCULAR FUNDUS. J. L. PAVIA, Arch. de oftal. de Buenos Aires **10:** 438 (June) 1935.

After referring to five cases which he has already reported Pavia presents a sixth case. He considers that the green spot is produced by a choroidal lesion that alters the chromatic aspect of the ophthalmoscopic field: The green color of the spot is more or less accentuated; the outlines of the spot are diffuse and irregular; the size ranges from ¼ to 1 papilla diameter; the retinal vessels course over it without change in direction or caliber and without branching. It is visible in the inverted image with ordinary illumination and in the upright image with the electric ophthalmoscope; it is visible also with Gullstrand's monocular or binocular ophthalmoscope and in chromoretinographs. It is not visible in the direct or the indirect image with red-free light or in panchromatic retinographs.

The differential diagnosis is fully discussed.

After abstracting his previous reports Pavia describes the sixth case in detail. The spot was situated below and external to the disk, and stereoscopic retinographs showed no surface elevation.

C. E. FINLAY.

Vision

ANISEIKONIA—A FACTOR IN THE FUNCTIONING OF VISION. A. AMES, Am. J. Ophth. **18:** 1014 (Nov.) 1935.

Ames discusses perspective and stereoscopic vision and how the latter is affected by aniseikonia (difference in relative size and shape of the two ocular images) and by declinations of the retinal meridians. He describes an instrument called the "tilting field." The normal person will set the tilting surface parallel to the frame. Sixty-five patients were tested after their aniseikonia had been measured and corrected, and not one showed a normal sense of depth. To 97 per cent of these subjects the plane appeared tilted in the direction indicated by the aniseikonia. They interpreted the orientation of surfaces, planes and groups correctly through their sense of perspective, which is little if at all affected by their aniseikonia.

W. S. REESE.

STELLAR VISION. A. POLACCO, Ann. di ottal. e clin. ocul. **64:** 81 (Feb.) 1936.

Polacco investigated several puzzling phenomena by means of photographs taken under various optical conditions and attempts to explain them. One of these is the phenomenon described by various astronomers as seen during the passage of a planet across the sun, which has been called the "black drop" or "chinese hat." By means of Gullstrand's bicylindric lens placed in a "prefocal" or "postfocal" position, with a screen, photographs of a point of light were made which were identical with this astronomical phenomenon. The various pictures described by different astronomers may probably be explained as due to different refractive conditions in the eyes of these observers.

S. R. GIFFORD.

Visual Tracts and Fields

MACULAR VISION FOLLOWING CEREBRAL RESECTION. J. FOX and W. GERMAN, Arch. Neurol. & Psychiat. **35:** 808 (April) 1936.

This report is an attempt to correlate the visual changes following resection of a known cerebral area with the anatomic knowledge of the course and termination of the geniculocalcarine pathway. The lesions studied involved (1) the temporal lobe, (2) the region of the angular gyrus and (3) the occipital lobe. Six cases are reported, and diagrams of the resected areas in the brain with the corresponding defects of the visual fields are shown. The authors conclude that the macular fibers in the inferior longitudinal fasciculus (geniculocalcarine pathway) are not solely confined to the central bundle but have a widespread distribution throughout the fasciculus. A similar arrangement occurs in the calcarine area, with some macular elements located as far forward as the anterior extremity of the area striata. This widespread representation of the macular fibers explains the frequent sparing of the macula in hemianopic defects and excludes the necessity for postulating bilateral macular representation. As far as the geniculocalcarine tract is concerned, it appears that macular splitting occurs only after complete section of the

tract, that is, of the inferior longitudinal bundle. As far as the termination area or optic radiation is concerned, splitting occurs only after resection in the posterior temporal region carried down to the ventricle and including the wall of the descending portion and the inferior segment of the temporal detour.

The discussion of this paper brings out interesting arguments but no contradictory evidence.

R. IRVINE.

Sympathetic Ophthalmia

SYMPATHETIC OPHTHALMIA. A. C. WOODS, Am. J. Ophth. **19:** 100 (Feb.) 1936.

Woods discusses the pathology of sympathetic ophthalmia and its resemblance to that of ocular tuberculosis. Blood changes cannot be regarded as important. Enucleation of the exciting eye within two weeks is recognized as, and has been proved to be, preventive. When it fails, the disease is usually relatively mild. After the onset of sympathetic disease enucleation is less useful but should be done if the eye is blind. The treatment consists in obtaining and maintaining mydriasis. The most valuable drug is sodium salicylate. Nonspecific protein therapy in the form of injections of diphtheria antitoxin is also of value, as is desensitization with uveal pigment. The result depends on how early the patient is seen and is favorable in 66 per cent of patients treated promptly.

W. S. REESE.

THE MENINGEAL REACTIONS OF SYMPATHETIC OPHTHALMIA. CORCELLE, Arch. d'opht. **52:** 327 (May) 1935.

Two cases are described in considerable detail which are thought to demonstrate meningeal involvement, although there were no neurologic signs. In one case deafness developed; in the other, vestibular hypoexcitability. The clinical aspect, prognostic value and therapeutic implications of meningeal reactions in this disease are briefly discussed. A theoretical discussion of the pathogenesis supports the idea that the causal agent is transmitted through the meninges. The meningeal reactions of the disease are discovered only if the spinal fluid is studied. Lymphocytosis and hyperglycorrhachia will be found. Evidence of vestibular involvement can be uncovered if searched for.

S. B. MARLOW.

Therapeutics

CRITICAL REVIEW AND THERAPY OF OCULAR TUBERCULOSIS. E. WERDENBERG, Klin. Monatsbl. f. Augenh. (supp.) **94:** 1, 1935.

The present state of ocular tuberculosis and its therapy are critically evaluated and discussed by Werdenberg in the thirty-three pages of this supplementary number. Valuable accounts of the author's personal observations and views are given, and a bibliography of recent publications is appended. The first chapter refers to the relation between

ocular and general tuberculosis. It contains a comparison between the frequency of tuberculous uveitis and that of choroiditis as found by Axenfeld and others and by Werdenberg. In the 1,100 eyes of the latter's 702 patients with ocular tuberculosis iridocyclitis occurred in 65 per cent and choroiditis in 20 per cent. The ages of puberty and the menopause furnish most of the patients. The tuberculin test is not always diagnostically reliable. An intra-ocular metastatic process is secondary to the general tuberculosis and dependent on the state of immunization of the organism. Ranke's system of tuberculosis is given due consideration. It is applicable to ocular tuberculosis. His division into three characteristic stages of development is discussed. Various forms of benign productive, malign exudative and hemorrhagic ocular tuberculosis and juvenile retinal periphlebitis are evaluated.

Werdenberg maintains that at present the diagnosis and therapeutics of this disease are based on recognition of the character of the disease, including (1) the divers pathologic forms it takes, (2) the primary intrathoracic pathologic origin and (3) the general tuberculosis. The first chapter is concluded with tables containing Werdenberg's modification of Turban's classification of pulmonary, ocular and general tuberculosis.

In the second chapter Werdenberg reports on his therapeutic experiences in high altitudes in connection with the roentgen rays, the use of tuberculin, general and local treatment and other therapeutic measures. A detailed description of the results obtained is added.

Some of Werdenberg's conclusions are these: Ocular tuberculosis as a part of general tuberculosis is incalculable in its course. The diagnosis remains probable as long as no tubercle bacilli have been found, and the tuberculin test can be used only with reference to the general pathologic picture. A definite law of correlation exists between the stages of immunization and the pathologic anatomic forms of development of tuberculosis. Pulmonary changes of a mild or moderate degree but rarely of a severe degree are found roentgenologically in association with ocular tuberculosis. Exhaustive roentgenologic examination of the thorax is essential. Progressive tuberculosis of the intrathoracic glands is a frequent cause. Hematogenous spreading follows as soon as these glands become inert as a barrier. Aside from immunobiologic causes the anatomic condition of the blood vessels and retarded intraocular circulation play a rôle in the origin of ocular tuberculosis. Parallels of ocular and pulmonary tuberculosis are described. Werdenberg stresses the favorable influence of the high altitude of Davos, Switzerland, on the therapy. The result of the treatment with tuberculin depends on whether there is indication for it and on the dosage. Tuberculin therapy is indicated in the compensated and contraindicated in the noncompensated condition. The most careful method is Sahli's subepidermal treatment.

Indication and contraindication of local roentgen therapy correspond to a large extent to those for tuberculin therapy. The best results have been obtained in cases of iridocyclitis, but the scope of this therapy is limited. Results of the combined use of tuberculin and roentgen therapy are reported, and the indications and contraindications of subconjunctival injection of saline solution are discussed.

The results observed by Werdenberg were evident as anatomic improvements in 54 per cent of cases of ocular tuberculosis, then as an improvement of the intrathoracic source of the disease, and as a decided increase of vision in 72 per cent of the affected eyes. The results of the treatments showed that the different curative factors are not effective in all cases; that they are individually indicated; that the use of all curative factors has to be resorted to, and that high altitude is a necessary factor in curing ocular tuberculosis and its pathologic source.

K. L. STOLL.

Society Transactions

AMERICAN OPHTHALMOLOGICAL SOCIETY

Seventy-Second Annual Meeting, Hot Springs, Va., June 1, 2 and 3, 1936

LOUIS S. GREENE, M.D., WASHINGTON, D. C., *President*

J. MILTON GRISCOM, M.D., PHILADELPHIA, *Secretary*

A SECOND GROUP OF CASES OF ARACHNODACTYLY. DR. RALPH I. LLOYD, Brooklyn.

This paper will be published in full, with discussion, in a later issue of the ARCHIVES.

TWINNING AND OCULAR PATHOLOGY, WITH A REPORT OF BILATERAL MACULAR COLOBOMA IN MONOZYGOTIC TWINS. DR. ARNOLD GESELL and DR. EUGENE M. BLAKE, New Haven, Conn.

This paper was published in the June 1936 issue of the ARCHIVES, page 1050.

ANOMALOUS OPHTHALMIC ARTERY WITH OCULAR SYMPTOMS. DR. ADOLPH O. PFINGST, Louisville, Ky.

This paper is published in full in this issue of the ARCHIVES, page 829.

LEIOMYOMA OF THE IRIS. DR. ALBERT D. FROST, Columbus, Ohio.

The presentation of a case which must be regarded as one of leiomyoma of the iris is of unusual interest because it brings into the realm of clinical diagnosis and observation an entity which has been confined largely to that of academic conjecture, discussion and controversy. Although a few cases have been reported as instances of leiomyoma of the iris, in most of these the pathologic diagnosis can be questioned, as the existence of such a tumor in the iris or ciliary body has been postulated for the most part on the basis that leiomyoma occurs in other types of smooth muscle.

In 1923 Verhoeff reported a case of leiomyoma of the iris and concluded from a review of the literature that this was the first instance in which the diagnosis was not open to question, since in their pathologic reports other investigators had failed to describe the results of differential staining. Verhoeff presented an excellent description of the pathologic aspects. Velhagen in 1933 described a case of leiomyoma of the ciliary body, and Bossalino in 1934 reported a similar case involving the ciliary body and iris.

The patient whose case I report was a married woman 46 years of age. The growth was about 1 mm. in depth and extended from the pupillary margin to a little more than half the width of the iris. There was no impairment of vision, and the patient had no subjective symptoms. The tumor gradually increased in size until it was about twice as large as when first noticed. After numerous consultations, the clinical diagnosis of sarcoma was agreed on, and the eye was enucleated in March 1935.

The pathologic diagnosis was leiomyoma of the iris. The tumor was composed of interlacing, closely packed bundles of spindle cells, with rod-shaped nuclei in palisade arrangement, eosinophilic cytoplasm and myoglia fibrils. Apparently the tumor arose from the sphincter of the iris and was of epiblastic origin.

Clinically it is impossible to differentiate this type of growth from sarcoma, and the diagnosis can be made only by microscopic study.

DISCUSSION

DR. F. H. VERHOEFF, Boston: Examination of the sections of this tumor convinced me that it is leiomyoma, but I am not sure that it is of epiblastic origin. I thought the tumor in my case was probably mesoblastic in origin. After partial removal of the tumor by another surgeon, my patient went for sixteen years before glaucoma developed secondary to recurrence of the tumor, necessitating enucleation. I am sorry to say I have not seen the patient since. Leiomyoma can become malignant, as illustrated by Dr. Terry in a case which he recently reported. His patient had an operation on the uterus, and nobody knew what the tumor was which was removed. Some years later a tumor developed in the orbit in relation to Müller's muscle; so one cannot be sure whether that tumor arose from Müller's muscle, or whether it was metastatic from the uterus. Its appearance was perfectly typical of leiomyoma, but it was not all removed, and it recurred. With recurrence it became less and less like leiomyoma, and at the last operation no one could have said it was leiomyoma, for it looked like malignant sarcoma. I think one san say that a tumor is leiomyoma only when it has all the typical characteristics and one finds myoglia fibers, as in this case.

DR. CLARENCE KING, Cincinnati: I saw this patient through the kindness of Dr. Frost about a month after he first observed the peculiar changes in the left iris. When the results of a detailed general examination and of laboratory tests proved negative, it was obvious that the lesion in the iris was not due to inflammation. I found myself unable to arrive at a definite conclusion as to its nature. If it was not due to inflammation it could only be a neoplasm. Theoretically, since a benign tumor of the iris is very rare, it should be malignant. Objectively, it did not present the appearance of malignancy. It was sharply circumscribed. The iris tissue around it was normal. It was not markedly pigmented. There was no interference with the muscle function of the iris. During the period in which I observed it, it showed no tendency to grow.

As the patient had excellent vision, it appeared to me that no harm would be done by keeping her under observation before deciding on a

radical intervention. It is generally agreed that the partial removal of such a growth for biopsy is contraindicated. As the growth later showed signs of extending, I am convinced that Dr. Frost was fully justified in the best interests of the patient in enucleating the eye. This case raises again the question as to whether iridectomy is ever indicated in sarcoma of the iris. Wintersteiner holds that iridectomy is indicated in cases in which the visual acuity is good and in which there is some prospect that it will remain useful after the operation. The tumor must be small, circumscribed, solitary, free, and situated in the pupillary zone of the iris. Iridectomy is contraindicated, according to him, in those cases in which the tumor involves the angle of the chamber if it impinges on the cornea or is adherent to the lens. According to Wintersteiner, of thirty-one patients who were treated for sarcoma by iridectomy, eighteen were cured and thirteen not cured after two years of observation.

Dr. Alan C. Woods, Baltimore: I saw this patient at a much later date than Dr. King did. At the time I saw her, the tumor was not circumscribed and was very definitely invasive. It did not involve the angle of the anterior chamber. To my mind, it had the characteristic appearance of sarcoma. It so happened we had seen several patients with sarcoma of the iris just before that, and the appearance in this case was practically identical with that in one or two patients with early cases I had seen. When the sections came back from Dr. Frost, I was frankly amazed at the picture. Dr. Jonas Friedenwald examined the sections and concurred fully in the diagnosis of leiomyoma made by Dr. Reese and Dr. Wheeler.

Dr. Albert D. Frost, Columbus, Ohio: I neglected to say that without the help of Dr. Wheeler and members of his staff I do not think I should have been able myself to arrive at this diagnosis; so I claim no credit for it.

Concerning the remarks of Dr. Verhoeff in regard to the epiblastic origin of this tumor, I concluded that since the sphincter and the dilator fibers of the iris are of epiblastic origin I might regard this tumor, since it appears to have come directly from those fibers, as having the same origin.

A Case of Hyperplasia of the Epithelium of the Ciliary Processes (Ciliary Adenoma of E. Treacher Collins). Dr. William Zentmayer, Philadelphia.

This paper was published in full in the October 1936 issue of the Archives, page 677.

Diphtheria of the Conjunctiva. Dr. S. Hanford McKee, Montreal, Canada.

A girl of 9 and a boy of 5 years were brought to the clinic, each with membranous conjunctivitis of one eye. In the smears microorganisms similar to the Klebs-Löffler bacillus were found and later such organisms were isolated in pure culture. In case 1 these microorganisms were morphologically and biochemically not typical; the

guinea-pig, however, left no doubt in the matter. In case 2 the microorganisms proved to have high virulence; in case 1 their virulence was mild. In both patients examination failed to reveal diphtheria of any other part.

DISCUSSION

DR. FRED T. TOOKE, Montreal, Canada: It may be interesting to report a case very comparable in many respects to the two reported by my colleague, Dr. McKee. A boy 2 years of age was a patient in the surgical wards of the Royal Victoria Hospital. We were called in to examine his left eye, which had become suddenly very swollen. The body temperature was 102 F. The lids were separated with very great difficulty, owing to the tremendous swelling, and a membrane such as Dr. McKee has described was found on the palpebral conjunctiva. Smears were made and diphtheroid organisms demonstrated. A Buller shield was applied over the right eye. The bacteriologist made a tentative diagnosis of diphtheria and later reported that the tests for virulence were positive. There was no evidence of diphtheria elsewhere in the body. The child was given 10,000,000 units of diphtheria antitoxin, and improvement followed in a most spectacular manner. The inflammation of the eyelid subsided entirely, and the temperature became normal. When I saw the child four days afterward, the eyelids were free from membrane and quite freely movable, and the cornea was clear.

OCULAR MUSCLE PALSIES IN A PATIENT WITH TOXIC GOITER. DR. CHARLES E. G. SHANNON, Philadelphia.

This paper concerns a case of toxic goiter with paralysis of the right and left superior recti and of the inferior oblique muscles, without exophthalmos. A modified O'Connor operation on the right superior rectus with tenotomy of the inferior rectus enabled the right eye to assume its normal position, with movements limited only in the superior field. Later a similar procedure was carried out on the left side. Binocular single vision was followed in a few days by diplopia, necessitating advancement of the internal rectus and recession of the external rectus on the right side and later recession of the superior rectus on the left side. With a 4 diopter prism in each eye the diplopia was overcome, and the patient was able to return to his work as a miner.

DISCUSSION

DR. ALAN C. WOODS, Baltimore: Last winter Dr. Thomas and I saw a patient in whom exophthalmos and palsy of the various ocular muscles came on two years after thyroidectomy, when the basal metabolic rate was normal and all signs of hyperthyroidism had disappeared. We went over our records to see how many patients with such a history we had had, and to our amazement we found that there had been sixteen in whom postoperative exophthalmos associated with ocular palsies came on when the thyroid disturbance was under control and there were no signs of myxedema. One patient had bilateral exophthalmos coming on about a year after thyroidectomy. The cornea became infected; both eyes were enucleated in another clinic. There was a

mass of hypertrophied tissue in the conjunctiva; she came to Baltimore with this huge mass of tissue protruding between both lids. To enable her to wear prostheses, we removed considerable orbital tissue, which on examination failed to show a tumor.

Marine has performed thyroidectomy on animals and by giving an extract of the posterior lobe of the pituitary gland has been able to produce definite exophthalmos in these animals. It looks as though the picture in hyperthyroidism represents simply a general syndrome, and as though the thyroid and ocular signs are not related to the thyroid toxin. They may well be related to the thyrotropic hormone. At any rate, as one analyzes these cases one has to look at them from an entirely different point of view, getting away from the idea that thyrotoxin may be responsible. The fact that in a number of cases this combination of symptoms appears when the metabolic part of the thyroid syndrome is controlled and when there is no evidence of myxedema, I think, points to a pituitary disturbance or to a thyrotropic hormone in some way.

Dr. Luther C. Peter, Philadelphia: Aside from the very remarkable symmetry of the paralysis in this case, including, as it does, the two superior recti and at the same time the inferior oblique muscles, I am especially interested in the corrective procedure with which Dr. Shannon has obtained such excellent results. It brings up the question whether it is ever advisable, even in the presence of a paralytic squint, to tenotomize a vertically acting rectus muscle. I have felt for a long time that the tenotomizing of a rectus muscle, even in the presence of a positive squint, is not advisable. On the other hand, I believe that if the inferior recti had been set back 3 or 4 mm. and at the same time had been displaced outward so as to balance the torsional action of the superior oblique muscles, there probably would have been less divergence of the eyes after the operation. If the inferior recti are tenotomized, there is practically but one muscle operating as a torsion muscle; that is the superior oblique. Setting the inferior recti back and at the same time displacing them outward would not only balance the torsional action of the superior oblique muscles but would at the same time correct the tendency to divergence.

Dr. Charles E. G. Shannon, Philadelphia: Replying to Dr. Peter, I might say that the technic of the operation consisted in exposing the external, internal and superior recti, splitting the two lateral recti and attaching the upper tongue of each to the superior rectus. Following these procedures, the superior rectus was advanced according to the Worth method, and the inferior rectus was tenotomized.

A Polarized Light Attachment for the Ophthalmoscope. Dr. John N. Evans, Brooklyn.

A compact and practical device is described, which can be attached to any standard model of the ophthalmoscope, and which permits examination of the ocular structures, particularly the eyeground, in polarized light. No attempt is made to describe in detail the changes noted or to interpret their significance.

CHOROIDAL CHORIONEPITHELIOMA SECONDARY TO TERATOMA OF THE TESTICLE. DR. ALEXANDER E. MACDONALD, Toronto, Canada.

This paper was published in full in the October 1936 issue of the ARCHIVES, page 672.

HEMANGIOMA OF THE CHOROID. DR. EMORY HILL, Richmond Va., and (by invitation) MAJOR RAYMOND O. DART, Washington, D. C.

A pathologic report of five eyes studied at the Army Medical Museum is presented, together with a brief discussion of the literature. The following conclusions are reached: Hemangioma of the choroid is not exceedingly rare, more than thirty cases having been definitely known. The condition is not diagnosed clinically. When a tumor is suspected, the clinical diagnosis is melanoma. Often a tumor is not suspected, and the eye is removed because of acute glaucoma. If all eyes enucleated for glaucoma were examined microscopically, it is likely that hemangioma would be found more often.

DISCUSSION

DR. F. H. VERHOEFF, Boston: The first case of this condition which I observed I reported with Quackenboss, and I described it as a case of cavernous hemangioma. Later a case was studied in my laboratory, which Love "worked up," and he convinced me that it was not one of cavernous hemangioma. Such tumors are really capillary angiomas. Other features are that separation of the retina occurs very early and that ossification in the choriocapillaris occurs frequently.

The thing which interests me most is the association of angioma of the choroid with vascular nevus of the face, often of the eyelid. There is no question that vascular nevi of the skin follow the distribution of nerves, and it seems to me that angioma of the choroid may also have a neurogenic association. It is remarkable how similar are all the specimens that I have seen; they differ only in size and in the ossification of the choriocapillaris. The tumors do not have to be very large before one observes complete separation of the retina.

DISCUSSION

DR. JOHN W. BURKE, Washington, D. C.: I saw this patient, with Dr. Hill, and wish to point out that transillumination showed thinning at the center of the tumor. The tumor reminded one of a red blood cell, with dense and sharply defined edges and yet with considerable transmission of light through the center. Transillumination might be a point in the differential diagnosis between a tumor of this type and a flat melanosarcoma.

DISCUSSION

DR. EMORY HILL, Richmond, Va.: I had never known of a case of hemangioma of the choroid in which the diagnosis was made clinically, nor had I ever received a report of such a tumor from a pathologist until these two cases came under my observation. It seems that the prospect for life in cases of intra-ocular tumor in adults is less hopeless than has been believed, since some growths of this type are not melanoma but benign vascular tumors. The end-result, so far as vision is con-

cerned, is the same. It is also possible, as Major Dart suggests, that angioma may escape the pathologist's notice and the diagnosis of "no tumor" be made, since the smaller growths collapse to the point of invisibility when the eye is opened in the laboratory.

BILATERAL METASTATIC CARCINOMA OF THE CHOROID: SUCCESSFUL ROENTGEN TREATMENT OF ONE EYE. DR. ALBERT N. LEMOINE, Kansas City, Mo., and DR. JOHN MCLEOD, Kansas City, Mo.

This paper is published in full in this issue of the ARCHIVES, page 804.

PLEXIFORM NEUROFIBROMATOSIS (RECKLINGHAUSEN'S DISEASE) INVOLVING THE CHOROID AND CILIARY BODY. DR. JOHN M. WHEELER, New York.

Although several cases of neurofibromatosis involving the choroid have been reported, there has never been a discussion of the subject of ocular involvement in a session of this society. In the present article points of interest in reported cases are referred to, and a case is reported. In a young girl with marked neurofibromatosis of the eyelids buphthalmos developed. The globe was enucleated, and frank involvement of the choroid and ciliary body was found.

DISCUSSION

DR. CONRAD BERENS, New York: I had the privilege of seeing this patient when she was only a day old. At that time the left cornea was 11.5 mm., and the right, only 8 mm. in diameter. There were a number of vessels on the iris in the right eye, and a few on the iris in the left eye. Because of the fact that Magitot had just published his reports of cases of congenital glaucoma, in which he had found infiltration around the vortex veins, I had Wassermann tests made on the child, the mother and the father, with negative results. I observed the child for several weeks, noting that the cornea enlarged rapidly. Dr. Cutler was consulted, and he advised operation. A 2 mm. trephine operation was performed in the right eye, and for several days the tension was lowered. I think Dr. Wheeler must have misunderstood my notes, for, in spite of the fact that there was some filtration, the tension rose again and remained elevated until the last time I saw the child, which was three or four months after that, when the family moved to Columbus and there placed the child in the care of Dr. Frost. At the request of Dr. Frost and the family I saw the baby two years later; the eyeball was greatly enlarged, and the orbit was enlarging rapidly. Dr. Frost believed that the presence of a tumor should be considered. Again we urged enucleation, but the family refused.

DR. F. H. VERHOEFF, Boston: There is one point in regard to the histology of these tumors which, I think, perhaps explains the pulsation which Dr. Wheeler referred to, and that is that they tend to become very vascular. One will find in one place a perfectly typical structure, with thickened nerves, which one recognizes very readily, and then one gets a piece of tissue with so few nerves in it that a mistaken diagnosis of angioma can readily be made.

Dr. Wheeler has discussed the one type which is very familiar, that of diffuse involvement of the choroid, with what appear to be nerve endings in it, and secondary glaucoma. But he does not refer to cases such as that reported by Major Callender. The eye described by Major Callender contained two tumors which ordinarily would have been described as spindle cell leukosarcoma—two isolated nodular tumors, one in the choroid and one in the iris or ciliary body—and one of these tumors in some of the sections could be traced into a nerve.

The chief condition from which it is difficult clinically to distinguish neurofibromatosis of the eyelid is lymphangioma, which gives a very similar appearance but lacks the cordlike feeling on palpation. Reliable differentiation is possible only by biopsy.

DISCUSSION

Dr. John M. Wheeler, New York: Dr. Berens asked about the microscopic observations with reference to the trephine operation. I did not have time to read all of Dr. Reese's report, but he describes sections through the trephine openings, and in these openings there were tags of iris, ciliary body and connective tissue, and there was neurofibromatous tissue adherent to that region.

Dr. Verhoeff's reference to pulsation ought to be spoken of. The pulsation I referred to has nothing to do with the histologic structure of the tumor. In any case in which a large part of the roof of the orbit has disappeared, the pulsation from the brain is transmitted through the orbit to the globe. This is seen in congenital defects of the orbit, outside the cases of neurofibromatosis. It is also seen postoperatively. In all the cases in which Naffziger has operated, removing the roof of the orbit, there has been pulsation of the globe.

Complications of the Forceps Intracapsular Operation for Cataract: Based on an Analysis of Five Hundred Successive Cases. Dr. Arnold Knapp, New York.

This paper is published in full in this issue of the Archives, page 770.

Further Observations on Detachment of the Choroid. Dr. C. S. O'Brien, Iowa City.

This paper was published in full in the October 1936 issue of the Archives, page 655.

Ocular Lesions in Postoperative Nutritional Deficiency. Dr. Henry P. Wagener, Rochester, Minn.

Optic neuritis (one case) and retrobulbar optic neuritis (two cases), each accompanied by neurologic manifestations, occurred as postoperative complications following general surgical procedures of different types. These neuritides are compared with similar syndromes which developed in two cases of pernicious vomiting of pregnancy. The suggestion is made that all these lesions were due to rapidly developing nutritional or vitamin deficiency.

DISCUSSION

DR. ARTHUR M. YUDKIN, New Haven, Conn.: Cowgill, in his book on vitamin B, points out that dietary deficiency disease is more prevalent in this country than statistics reveal. The experimental work on the vitamins and the allied substances, the hormones, has made it possible for the clinician to interpret some of the obscure and refractory maladies that are encountered in the practice of medicine. It is regrettable that a good deal of the present knowledge of vitamins is obtained from pharmaceutical brochures and so-called detail men rather than from original sources. Experimental investigation reveals that vitamins are merely a supplement and should be used in conjunction with a well balanced diet.

DR. HENRY P. WAGENER, Rochester, Minn.: The simple use of the vitamins alone does not entirely cure these conditions. In reading the reports of these cases more in detail it will be observed that final improvement took place only after the patients were able to take and absorb a well balanced diet with vitamin supplements added.

FUNDUS AND FIELD CHANGES IN CLOSURE OF THE RETINAL ARTERY. DR. ARTHUR J. BEDELL, Albany, N. Y.

Critical analysis and careful inspection of photographs and fields show that:

1. There is a definite field defect in the form of a straight line even when the edematous retina presents a crenate border.

2. The macula may be partly encircled and yet central vision be retained.

3. An embolus may be visible at the apex of the white region of retinal edema which coincides with the part of the retina supplied by that particular artery.

4. A field defect suggesting a raphe is present, is readily recognized and has frequently been recorded.

5. The review of cases which is presented in this paper shows that the majority of the patients complained of sudden loss of vision without premonitory obscurations.

6. Some of the occlusions are definitely coincident with cardiac disease and others with hypertension.

7. After a vessel has once been occluded it seldom, if ever, reopens, but remains as a visible white line.

This subject is presented in the expectation that the method of studying photographs and fields in parallel will be adopted universally, so that more definite information can be obtained regarding the part of the retina supplied and the decrease of its function following lack of nourishment. The advantages of this method are many: Since all clinicians can use it, more cases will be observed and more accurate deductions finally drawn, whereas if reports are confined to pathologic examinations they fail of accuracy because such examinations are almost always made long after the vascular accident, at a time when the eyes usually exhibit other degenerative changes. The scheme outlined offers immediate, direct evidence, whereas the older method gave delayed, sometimes conjectural conclusions.

DISCUSSION

DR. HENRY P. WAGENER, Rochester, Minn.: The first point which Dr. Bedell mentioned has always been very interesting to me. In the closure of the central artery or of its branches which is seen early but not immediately after the incident there is no apparent narrowing of the lumen. The narrowing apparently comes on much later and becomes definitely visible only after the ischemic area of the retina has disappeared. It is extremely interesting how little residual change may be visible in the arterial wall after such a closure; so that often one first suspects that there has been a closure only because one sees a field defect of the type which Dr. Bedell has presented. A careful estimation of the relative sizes of the arteries in the two eyes will then demonstrate that the field defect corresponds to a narrowed vessel, which has been previously occluded.

I have been much interested in the nature of the plugs which Dr. Bedell has shown in his photographs. I have always tended to assume that such a plug represents an embolus in the lumen of the vessel. It is true, however, that in any number of the cases it is not possible to demonstrate any very good source of emboli, and I wonder whether some of the plugs can be produced by atheromatous degeneration of mural thrombi.

DR. ALEXANDER E. MACDONALD, Toronto, Canada: About three years ago, I observed an unusual change in the fundus of a woman with a systolic pressure of 240 mm. of mercury. Just underneath the macula there was a small arterial twig passing up toward the fovea. This was crossed by a branch of the lower temporal vein. The plug was seen at this crossing. There was considerable exudate there, as well as a very dark mass in the region of the fovea. It is probably a question of differentiation between an embolus and a lesion in the wall of the vessel.

DR. JOHN W. BURKE, Washington, D. C.: About five years ago I observed in my associate, Dr. Grear, a collapse in the upper temporal branch of the central artery of his better eye, the other eye having been damaged by injury in early youth. My associates and I saw him within thirty minutes after the subjective visual disturbance. No edema had occurred at that time. His field showed a nasal defect, and an embolus could be seen closing the branch mentioned. It was about 4 disk widths from the disk. The blood was not flowing through one branch and only trickling through the other. We immediately performed paracentesis and gave him a dose of amyl nitrate. By watching with the ophthalmoscope we could see the blood flowing through the branch a little better. We punctured the eye again and gave the patient another dose of amyl nitrate. He recovered without any loss of vision. The fact that he was attended by an ophthalmologist who recognized his symptoms and gave him immediate treatment was responsible for the good result in this case.

DR. JOHN N. EVANS, Brooklyn: I hope that in his paper Dr. Bedell goes into the details of taking the fields, because I believe there are two entirely different forms of technic to use in a study of this problem. One is limited to determining decreased circulatory efficiency, and the

other to determining decreased fiber bundle efficiency, and to me his charts appear as though his efforts had been limited to the latter method. I think his results would have been different had his technic been of a nature directed to both aspects of the problem.

DR. ARTHUR J. BEDELL, Albany, N. Y.: In answer to Dr. Evans' question as to the method by which the fields were taken, they were made with the Ferree-Rand instrument because I wished to show the gross field defects and not the more confusing outline made on the instrument of which he is the master.

I am especially grateful to Dr. Wagener for his remarks, because when he speaks on fundus changes ophthalmologists stop, listen and learn.

Dr. MacDonald's case can be paralleled in the experience of most of the members. The small arteries which supply the macular region are frequently involved in an arteriosclerotic process. A single vessel may become a white thread, or many branches may show such alterations. Localized white swellings, true enlargements are, I believe, arteriosclerotic plaques. They are quite different in appearance from a plug, which is within the vessel. By use of the modern ophthalmoscope and the various filters, particularly the red-free and the red light, it is possible to localize the lesion in the wall of the vessel or within its lumen accurately.

In reference to Dr. Burke's patient, I have never seen an embolus modified by any form of treatment. I have seen conditions which gave the symptoms of embolism but were later proved to be spasms, not occlusions. The correlation of fundus and field is extremely interesting.

I am said to be too enthusiastic regarding photographs. Perhaps I am, yet I notice that more and more ophthalmologists take pictures, and I am certain that more and more of them profit thereby.

HUMORAL BIOPATHOLOGY AND THE EYE: SOME INFERENCES AND IMPLICATIONS. DR. PERCY FRIDENBERG, New York.

The paper presents a general survey of the glands of internal secretion, the vegetative nervous system, vitamins and some factors of metabolism, in relation to the eye, its development, structure and function in health and disease. Comment is made on the clinical features of ocular disease associated with constitutional symptoms of endocrine imbalance and on typical dyscrinisms with ocular manifestations. Mention is made of categories, such as sex and age, and their biologic implications; physique, form of skull and ocular correspondence; the connection of the eye with the endocrine glands via the vegetative nervous system, suggesting a secretogenic factor in oculosomatic reactions such as eye strain and migraine, in line with Cannon's theory of the emotions.

A STUDY OF THE CHANGES IN THE OPTIC DISKS, VISUAL FIELDS AND VISION FOLLOWING BISECTION OF THE OPTIC CHIASM. DR. HENRY C. HADEN, Houston, Texas.

Following an operation at which it was necessary for a brain surgeon to bisect the optic chiasm in order to remove part of a craniopharyngeal

cyst there was gradual loss of color in the uncupped portions of the disk occupied by the crossed fibers of the optic nerve. This continued until only a small area in the upper portion and one in the lower portion of each optic disk, that is, the portion occupied by the uncrossed fibers, remained pink.

The patient suffered from loss of weight and strength, low blood pressure, low basal metabolic rate, subnormal temperature, polyuria and nocturia. The vision which she had through the uncut fibers of the nerve gradually failed.

On the administration of whole pituitary hypodermically and by mouth, her strength, weight, blood pressure and basal metabolic rate increased, polyuria disappeared, and vision improved.

As long as whole pituitary was administered she did well and vision was sustained; but when it was omitted, her vision, as well as her general physical condition, failed.

DISCUSSION

DR. F. H. VERHOEFF, Boston: It does not seem to me that one can conclude from this case that if one injured the optic nerve it would take almost three months for the disk to show pallor. I think the character of the injury has a great deal to do with the length of time it takes. Of course, the optic nerve fibers still have their ganglion cells, and in other nerves one does not cause atrophy when one cuts the nerve if it is still connected with its ganglion cell. In this case, trauma to the optic nerve in some way injured the ganglion cells—trauma done with a sharp knife—and this would be different from that which occurs when the optical canal is crushed or in other conditions.

DR. THEODORE L. TERRY, Boston: This report is of great interest because the exact time the chiasm was severed is known. One sees lesions of the chiasm which give rise to bitemporal hemianopia and corresponding atrophy of the optic nerves, but the time at which the chiasm was destroyed is not known. In certain other instances the period of time elapsing between the destruction of the nerve and the appearance of atrophy is known. In one instance an optic nerve was almost completely severed by a buttonless fencing foil. The eyeball was not injured. Optic atrophy was evident in a little less than six weeks. In another instance optic atrophy was not evident four weeks after the occurrence of blindness due to malignant tumor just behind the orbit. The exact time of the blindness was presumed to be when the patient noticed cessation of diplopia, the diplopia being due to paralytic strabismus.

Certainly, the more malignant type of tumor can destroy the optic nerve completely before any optic atrophy is seen with the ophthalmoscope, whereas the slow destruction of the nerve by a benign tumor would probably result in evidence of atrophy before the entire nerve was destroyed. Therefore, the presence or absence of optic atrophy may be of clinical value as well as of aid in medicolegal cases.

CHRONIC TRAUMATIC SUBDURAL HEMATOMA AS A CAUSE OF CHOKED DISK. DR. CLARENCE KING, Cincinnati.

Frequent references occur in the general literature to the type of patient in whom symptoms of intracranial pressure develop at varying

intervals after a trauma to the head, and who is found, either at operation or at autopsy, to have an organizing blood clot beneath the dura. Ocular symptoms, especially choked disk, are frequently observed in connection with chronic subdural hematoma. Despite this fact, no significant consideration has been given to it in the ophthalmic literature. Not infrequently such a patient first seeks relief at the hands of the ophthalmologist or is referred to him in consultation. If a subdural hematoma is recognized or even if it is suspected to be present, appropriate surgical intervention often results in a complete cure. If the condition is unrecognized and therefore not properly treated, permanent disability or death may ensue. I report a case of chronic subdural hematoma with choked disk, together with the salient features of such growths as described in the literature.

DISCUSSION

DR. WALTER I. LILLIE, Philadelphia: Dr. King has presented a very interesting case from a diagnostic standpoint. Unilateral choked disk in association with blurred vision is rather unusual, because choked disk in itself does not produce visual changes until the onset of secondary optic atrophy. To me this visual change suggests a relative central scotoma, which might be due to the edema spreading to the macula or to the early phase of the Gowers-Paton-Kennedy syndrome. Surgical procedure has shown it was subdural hematoma over the cerebrum, so apparently the frontal or middle fossa was not affected.

Choked disk in association with subdural hematoma is rare rather than common, and I think this perhaps explains why there has not been much about subdural hematoma in ophthalmic literature. When choked disk occurs it occurs late in the course of the disease, and neurologists or the neurosurgeons have had difficulty in locating the lesion accurately. In my experience, choked disk is very rare except in relation to a hematoma that has become expansile. This case is of greater interest because of the unilateral choked disk associated with hematoma.

In the cases I have seen the condition is much more easily diagnosed through neurosurgical procedures such as encephalography than by ventriculography, because the cerebrospinal fluid flowing beneath the dura seems from the encephalogram to spread up over the temporal region and the cortex. The normal spaces are obliterated and the neurosurgeon makes a diagnosis quite readily, while from the ophthalmologic standpoint one usually sees nothing. I suggest making an encephalogram rather than a ventriculogram, as the mortality with encephalograms is practically nil. The neurosurgeon is then forewarned and can choose between using a trephine and making an osteoplastic flap to remove the blood clot.

DR. L. T. POST, St. Louis: Furlow reported (*Arch. Surg.* 32: 688 [April] 1936) sixteen cases of subdural hematoma from the neurosurgical service of Washington University, St. Louis, in which the incidence of choked disk was 68 per cent. The amount of choking is usually low.

Of the sixteen patients, six died but five of these were brought to the hospital in a state of coma.

I am not sure whether Dr. King mentioned that one of the interesting features is the latent period during which there may be absence of symptoms and following which the patient may suddenly become unconscious.

Another typical case was seen in the same service a month ago. Since this number of cases can be seen in one service, the condition must be less rare than is generally thought, and its presence should be considered as a possibility in a case of choked disk.

Dr. Thomas H. Johnson, New York: It seems to me that with subdural hematoma the presence of papilledema will depend on the size and location of the hemorrhage. It must be of sufficient size and in a location to interfere with the drainage of the cerebrospinal fluid from the cranial cavity so that intracranial pressure is produced. I have encountered a considerable number of cases of papilledema, and a very common early symptom is subjective visual disturbances, although the central vision may be normal.

DISCUSSION

Dr. Clarence King, Cincinnati: In response to Dr. Lillie's inquiry concerning the central scotoma, my associates and I looked very carefully for it, and we could not believe there was none, but none was found.

In regard to the incidence, this survey of 244 cases is not sufficient to give an idea as to that. Perhaps a further survey would indicate that the condition is rather rare, but it was found in 44 per cent of this series of 244 cases.

In regard to Dr. Post's comment about the interval during which the lesion is latent, I did mention that in the paper. This interval is quite characteristic. It is difficult to explain why there should be such a long interval in some cases. It is sometimes years, and for that reason I mentioned the expansion of the tumor by osmosis as an explanation, but that terminates at the end of a few months, and why after months, sometimes years, there is an expansion is as yet unknown. It may be due to hemorrhages, as explained by Leary.

Dermoid Cysts of the Orbit. Dr. Bernard Samuels, New York.

This paper is published in full in this issue of the Archives, page 776.

Neosynephrin Hydrochloride: Some Uses and Effects in Ophthalmology. Dr. Parker Heath, Detroit.

This paper is published in full, with discussion, in this issue of the Archives, page 839.

Book Reviews

The Eye and Its Diseases. By Eighty-Two International Authorities. Edited by Conrad Berens, M.D., Ophthalmic Surgeon, Pathologist and Director of Research, New York Eye and Ear Infirmary; Special Consulting Ophthalmologist, Woman's Hospital; Lieutenant-Colonel, M. R. C., U. S. A. Price, $12. Pp. 1254, with 436 illustrations, some in colors. Philadelphia: W. B. Saunders Company, 1936.

The title of this work suggests, and the preface informs one, that its aim is to present the essentials of ophthalmology to physicians, surgeons, neurologists, medical students and those entering the practice of ophthalmology, to give an account of the more important recent advances in the art and science of this specialty and, in general, to put in the hands of the reader, whether neophyte or expert, a practical reference book. To this end over fourscore specialists of repute, American and European, have contributed almost as many chapters to a stately volume in which their treatises have been combined and arranged by the talented and ambitious editor, who himself has translated a number of the presentations and contributed the section on the surgery of the eye. These chapters take in a field which includes not only the diseases, but also the embryology, biology, heredity, injuries and comparative anatomy, of the eye and its relation to the nervous system, immunology and hygiene. They deal also with the history of ophthalmology, its medico-legal aspects, social-economic and educational implications and, last but not least, laboratory diagnosis, including pathologic and bacteriologic technic. In scope and inclusiveness, as well as in multiple authorship, this work has all the features of a system of ophthalmology rather than those of a textbook on diseases of the eye.

An introductory chapter, by Thomas Hall Shastid, presents the history of ophthalmology in an interesting but sketchy résumé of the contributions of oculists from Hammurabi to Dennet. One misses an account of the evolution, throughout the ages, of the science itself as a whole and of such important details as the theories of glaucoma, vision, operation for cataract, and so on. There are, however, historical notes in some of the other chapters, notably that on ophthalmoscopy, by LeGrand Hardy, which also presents the optical principles and the practical technic of this procedure in an understandable yet scientific and complete manner. The anatomy of the orbit and of the eyeball and its adnexa is detailed by S. E. Whitnall and beautifully illustrated. Ida Mann supplies a much condensed account of the antenatal and postnatal development of the human eye. Other summarizing chapters deal with medical ophthalmology (R. Foster Moore), tuberculosis of the eye (Finoff), ocular syphilis (J. Herbert Waite), the physiology of the eye (Jackson) and that of vision (John Evans), the general pathology of the eye (Greeves), the hygiene of the eye (Alger), immunology in ophthalmology (Alan Woods) and medical jurisprudence in ophthalmology (Shastid). The basic principles of ophthalmic surgery are presented by the editor him-

self, and the procedures in local anesthesia are described, rather too briefly, by O'Brien. Separate sections are devoted to operations on the lids (Spaeth), the lacrimal apparatus (John E. Weeks), the lens (Blake), the ocular muscles (Lancaster) and other structures. Among a number of excellent chapters by foreign colleagues are that on peripheral vision and perimetry, by Traquair; on slit lamp and corneal microscopy, by Rehsteiner; on trachoma, by Lindner, and on diseases of the optic nerve, by Van der Hoeve, and an outstanding presentation of diseases of the cornea, with an account of methods of examination and very instructive illustrations, by Basil Graves. Operations on the retina are discussed by Marc Amsler; those for glaucoma, by Lister, and procedures for the removal of foreign bodies, by Comberg.

To have brought all this material into the compass of a single volume of standard size is, in itself, a remarkable performance. If the result had been perfection it would have been a miracle. The surprising thing is not that the work falls short of that ideal but that, taken all in all, it is so satisfactory and, in many respects, excellent. It has the defects of its quality or, rather, of its quantity, and one has the impression that some chapters have, perhaps necessarily, been too greatly abbreviated or summarized. One or two are concise to the point of laconism, and this has caused, if not lacunae, at least a sort of bare bones presentation in which enumeration, cataloging or a system of general reference has taken the place of that analysis, discussion and critique which make the classic treatises and the great *Sammel-Werke* so valuable. This judgment does not apply by any means to all the contributions, as many authors present their topic in extenso and most instructively. But the result is a certain unevenness in scope and presentation. This applies even to the illustrations, some of which are excellent, for instance, those presenting the gross anatomy of the eyeball and the diagrams illustrating focal and slit lamp examination of the cornea, anterior chamber and lens. Others, especially the reproductions of histologic sections and of photographs of instruments, are often on so small a scale that important details escape observation. An unusually complete and well arranged index is a feature of the work, which by numerous cross-references to subjects and authors greatly facilitates looking up any particular topic. Most of the chapters also have appended an extensive bibliography. The student, the practitioner or the specialist who consults this work cannot fail to add greatly to the store of his knowledge and to profit thereby. He will learn something about everything important connected with ophthalmology. He must not expect to learn everything about anything.

PERCY FRIDENBERG.

Proceedings of the All-India Ophthalmological Society. Volume IV: Session 1935. Pp. 279. Madras: Madras Publishing House, Ltd., 1936.

This volume opens with the report of a symposium on nutritional disorders of the eye. The first paper, entitled "Eye Diseases Due to Improper Diet," by Lieutenant-Colonel Sir J. N. Duggan and B. P. Nanavati, gives an excellent summary of ocular disorders due to lack of vitamins A, B, C and D, as well as disorders due to a dietary excess of carbohydrate and contamination of food and gout and rheumatism.

Other papers of the symposium are concerned with malnutrition, xerophthalmia, keratomalacia, night blindness and the ocular disorders of diabetes.

In his paper entitled "A Short History of the Incidence of Glaucoma in Bengal" Captain S. C. Dutt notes that the established signs and symptoms of glaucoma associated with epidemic dropsy (Bengal glaucoma) are: (1) a high intra-ocular tension averaging from 70 to 100 mm.; (2) a normal or a deep anterior chamber; (3) absence of pain; (4) absence of congestion; (5) a normal and active pupil in most cases; (6) gradual loss of the field of vision, with the usual subjective symptoms, a cupped disk, and striking pallor of the disk, as in the usual type of glaucoma seen in the Occident. A well performed trephination usually halts the disease and gives relief. As epidemic dropsy is limited to the region of Bengal, it is probably due to the ingestion of a particular kind of rice. Both epidemic dropsy and the glaucoma associated with it are probably due to an increased permeability of the capillaries, which may be toxic or dietary in origin.

As forty papers were read at this meeting, it is impossible to give even the titles of all in the space allotted this review. The volume contains much of interest, especially in those papers dealing with extraction of cataract, a field in which ophthalmologists in India have practically unlimited opportunities for comparing the various types of operations.

The presidential address was made by Lieutenant-Colonel Robert Wright. Lieutenant-Colonel E. O'G. Kirwan is president elect for the next session of the society.

W. F. DUGGAN.

History of the Ophthalmologic Clinic No. 2 of the Kharkof Medical Institute, Kharkof, U. S. S. R. Dr. E. B. Rabkin, Director. Pp. 57, 1936.

This clinic was founded in 1910 and was conducted by Professor Braunstein from 1910 to 1926, by Prof. P. P. Prokopenko from 1926 to 1928 and since 1932 by Dr. E. B. Rabkin.

The clinic was first transferred to the Professor Hirshman Memorial Eye Hospital. It had thirty beds and was equipped with all the latest instruments for clinical ophthalmology. A number of scientific questions were investigated, and work in social hygiene was also done.

In 1928 the eye clinic was merged with the Eye Clinic No. 1 of the Kharkof Medical Institute, and in 1932 it ceased to function as an independent clinic when it became the Ukrainian Ophthalmological Scientific Research Institute. Later it was again returned to the Kharkof Institute and now has been reorganized as Clinic No. 2 for Eye Diseases of the Kharkof Medical Institute. It has a good library, good laboratory facilities and a roentgen department and is well fitted for the instruction of undergraduates and graduates and for the pursuit of scientific research. Scientific conferences are held at regular intervals, at which papers are read and patients demonstrated.

ARNOLD KNAPP.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Prof. F. de Lapersonne, 217 Faubourg St. Honoré, Paris.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.

International Ophthalmologic Congress

Secretary: Dr. E. Marx, Costzeedijk 316, Rotterdam, Holland.
Place: Cairo. Time: December 1937.

FOREIGN

British Medical Association, Section on Ophthalmology

President: Dr. P. E. H. Adams, 6, Holywell, Oxford.
Secretary: Dr. Thomasina Belt, 13, Mitchell Ave., Jesmond, Newcastle-on-Tyne.

Ophthalmology Society of Bombay

President: Dr. D. D. Sathaye, 127 Girgaum Road, Bombay 4.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

Ophthalmological Society of the United Kingdom

President: Mr. Gordon M. Holmes, 9, Wimpole St., London, W. 1.
Secretary: Mr. J. D. M. Cardell, 27, Weymouth St., London, W. 1.

Oxford Ophthalmological Congress

Master: Dr. C. G. Russ Wood, Hill House, Abberbury Rd., Iffley, Oxford, England.
Hon. Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England

Royal Society of Medicine, Section of Ophthalmology

President: Dr. Ransom Pickard, 31, East Southernhay, Exeter, England.
Secretary: Dr. A. Rugg-Gunn, 35, Harley St., London, W. 1.

Société Française d'Ophthalmologie

Secretary: Dr. René Onfray, 6 avenue de la Motte Picquet, Paris 7è.

Society of Swedish Ophthalmologists

President: Prof. F. Berg, Uppsala, Sweden.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 III tr., Stockholm, Sö., Sweden.

German Ophthalmological Society

President: Prof. Lohlein, Jena.
Secretary: Prof. A. Wagenmann, Heidelberg.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen, Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

Tsinan Ophthalmological Society

Chairman: Dr. Eugene Chan, Cheeloo University School of Medicine, Tsinan, Shantung.
Place: Cheeloo University School of Medicine. Time: Last Thursday of alternate months.

NATIONAL

American Medical Association, Scientific Assembly, Section on Ophthalmology

Chairman: Dr. William L. Benedict, 102 Second Ave., S. W., Rochester, Minn.
Secretary: Dr. Parker Heath, 1553 Woodward Ave., Detroit.
Place: Atlantic City. Time: June 7-11, 1937.

American Academy of Ophthalmology and Otolaryngology

President: Dr. Frank E. Burch, 408 Peter St., St. Paul.
Executive Secretary-Treasurer: Dr. William P. Wherry, 1500 Medical Arts Bldg., Omaha.

American Ophthalmological Society

President: Dr. Harry Friedenwald, 1212 Eutaw Pl., Baltimore.
Secretary-Treasurer: Dr. J. Milton Griscom, 2213 Walnut St., Philadelphia.

National Society for the Prevention of Blindness

President: Mr. William Fellowes Morgan, 50 W. 50th St., New York.
Managing Director: Mr. Lewis H. Carris, 50 W. 50th St., New York.

SECTIONAL

Central Wisconsin Society of Ophthalmology and Otolaryngology

President: Dr. E. S. Schmidt, 107 E. Walnut St., Green Bay.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.
Place: Eau Claire. Time: Nov. 6 and 7, 1936.

New England Ophthalmological Society

President: Dr. James J. Regan, 520 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. William P. Beetham, 5 Bay State Road, Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

Pacific Coast Oto-Ophthalmological Society

President: Dr. A. J. Ridges, Walker Bldg., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Frederick C. Cordes, 384 Post St., San Francisco.
Place: Salt Lake City, Utah. Time: May 24-27, 1937.

Puget Sound Academy of Ophthalmology and Oto-Laryngology

President: Dr. L. H. Klemptner, 509 Olive St., Seattle.
Secretary-Treasurer: Dr. Purman Dorman, Virginia Mason Hospital, Seattle.
Place: Seattle. Time: January 1937.

Rock River Valley Eye, Ear, Nose and Throat Society

President: Dr. A. H. Pember, 500 W. Milwaukee St., Janesville, Wis.
Secretary-Treasurer: Dr. W. H. Elmer, 321 W. State St., Rockford, Ill.
Place: Rockford, Ill., Janesville or Beloit, Wis. Time: Third Tuesday of each month.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Robert Griswell, 707 Washington Ave., Bay City, Mich.
Secretary-Treasurer: Dr. W. K. Slack, 308 Eddy Bldg., Saginaw, Mich.
Place: Saginaw, Mich., or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

SIOUX VALLEY EYE AND EAR ACADEMY

President: Dr. L. H. Hohf, Yankton, S. D.
Secretary-Treasurer: Dr. J. C. Decker, Francis Bldg., Sioux City, Iowa.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. William A. Wagner, 914 American Bank Bldg., New Orleans.
Secretary: Dr. O. M. Marchman, Medical Arts Bldg., Dallas, Texas.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. O. B. McGillicuddy, 1908 Capitol Band Tower, Lansing, Mich.
Secretary-Treasurer: Dr. Maurice C. Loree, 120 W. Hillsdale St., Lansing, Mich.
Time: Third Thursday of alternate months.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Leslie R. Hazlett, 100 S. Main St., Butler.
Secretary-Treasurer: Dr. C. W. Beals, 41 N. Brady St., DuBois.

STATE

COLORADO OPHTHALMOLOGICAL SOCIETY

President: A presiding officer is selected for each meeting alternately until all members have served.
Secretary: Dr. Edna M. Reynolds, 227, 16th St., Denver.
Place: Capitol Life Building, Denver. Time: 7:30 p. m., third Saturday of the month, October to April, inclusive.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Walter L. Hogan, 750 Main St., Hartford.
Secretary-Treasurer: Dr. Shirley H. Baron, 309 State St., New London.
Time: May, November.

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President: Dr. B. H. Minchew, 701 Elizabeth St., Waycross, Ga.
Secretary-Treasurer: Dr. Edward S. Wright, 1001 Medical Arts Bldg., Atlanta, Ga.

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. J. R. Dillinger, French Lick.
Secretary: Dr. Frederick V. Overman, 705 Hume-Mansure Bldg., Indianapolis.

IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. James A. Downing, 406 Sixth Ave., Des Moines.
Secretary-Treasurer: Dr. O. L. Thorburn, 213½ Main St., Ames.
Place: Des Moines.

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Parker Heath, 1553 Woodward Ave., Detroit.
Secretary: Dr. D. R. Heetderks, 26 Sheldon Ave., S. E., Grand Rapids.

Minnesota Academy of Ophthalmology and Oto-Laryngology

President: Dr. William L. Benedict, Mayo Clinic, Rochester, Minn.
Secretary-Treasurer: Dr. Walter E. Camp, 1918 Medical Arts Bldg., Minneapolis.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. Edward S. Murphy, Northern Pacific Hosp., Missoula.
Secretary: Dr. A. W. Morse, 507 Phoenix Bldg., Butte.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr. C. Coulter Charlton, 124 S. Illinois Ave., Atlantic City.
Secretary: Dr. H. L. Harley, 124 S. Indiana Ave., Atlantic City.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. John F. Fairbain, 925 Delaware Ave., Buffalo.
Secretary: Dr. Walter S. Atkinson, 168 Sterling St., Watertown.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. Burton W. Fassett, Geer Bldg., Durham.
Secretary-Treasurer: Dr. Casper W. Jennings, 332 N. Elm St., Greensboro.
Place: Durham. Time: Oct. 8, 1936.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. Trygve Oftedal, 55½ Broadway, Fargo.
Secretary-Treasurer: Dr. F. L. Wicks, 514 6th St., Valley City.

Oregon Academy of Ophthalmology and Oto-Laryngology

President: Dr. A. B. Dykman, Medical Dental Bldg., Portland.
Secretary-Treasurer: Dr. Andrew J. Browning, 418 Mayer Bldg., Portland.
Place: Good Samaritan Hospital. Time: Third Tuesday of each month.

Rhode Island Ophthalmological and Otological Society

Acting President: Dr. Nathan Bolotow, 108 Waterman St., Providence.
Secretary and Treasurer: Dr. Gordon J. McCurdy, 122 Waterman St., Providence.
Place: Rhode Island Medical Library. Time: 8:30 p. m., second Thursday in October, December, February and April.

South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. R. E. Houston, 103 E. North St., Greenville.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville.

Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. W. W. Potter, 601 Walnut St., Knoxville.
Secretary-Treasurer: Dr. W. D. Stinson, 248 Madison Ave., Memphis.

Texas Ophthalmological and Oto-Laryngological Society

President: Dr. T. E. Fuller, 100 W. Board St., Texarkana, Texas.
Secretary: Dr. O. M. Marchman, 1719 Pacific Ave., Dallas.
Place: Fort Worth. Time: Dec. 11 and 12, 1936.

Utah Ophthalmological Society

President: Dr. V. P. White, 143½ S. Main St., Salt Lake City.
Secretary-Treasurer: Dr. E. B. Fairbanks, Boston Bldg., Salt Lake City.
Time: Third Monday of each month.

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President: Dr. Emory Hill, 501 E. Franklin St., Richmond.
Secretary-Treasurer: Dr. George G. Hankins, Medical Arts Bldg., Newport News.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. F. O. Marple, First Huntington National Bank Bldg., Huntington.
Secretary: Dr. J. E. Blaydes, First National Bank, Bluefield.

LOCAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. B. E. Failing, 31 Lincoln Park, Newark, N. J.
Secretary: Dr. A. Russell Sherman, 671 Broad St., Newark, N. J.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. L. E. Brown, Second National Bldg., Akron.
Secretary-Treasurer: Dr. C. R. Andersen, First-Central Tower, Akron.
Time: First Monday in January, March, May and November.

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. William O. Martin Jr., 478 Peachtree St., Atlanta, Ga.
Secretary: Dr. A. V. Hallum, 478 Peachtree St., Atlanta, Ga.
Place: Academy of Medicine, 38 Prescott St. Time: Second Friday of each month from October to May.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Jesse W. Downey Jr., 529 N. Charles St., Baltimore.
Secretary: Dr. Mary L. Small, 18 W. Read St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to May.

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President: Dr. Walter V. Moore, 1 Nevins St., Brooklyn.
Secretary-Treasurer: Dr. Mortimer A. Lasky, 1 Nevins St., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

BUFFALO OPHTHALMOLOGIC CLUB

President: Dr. Thurber LeWin, 112 Linwood Ave., Buffalo.
Secretary-Treasurer: Dr. Meyer H. Riwchun, 367 Linwood Ave., Buffalo.
Time: Second Thursday of each month.

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Each member, in alphabetical order.
Secretary: Dr. A. H. Benz, 706 Medical Arts Bldg., Chattanooga.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

CHICAGO OPHTHALMOLOGICAL SOCIETY

President: Dr. Robert B. Blue, 25 E. Washington St., Chicago.
Secretary-Treasurer: Dr. Thomas D. Allen, 122 S. Michigan Ave., Chicago.
Place: Medinah Michigan Avenue Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati Ophthalmic Club

Chairman: Each member, in rotation.
Secretary-Treasurer: Dr. E. R. Thomas, 819 Carew Tower, Cincinnati.
Place: Holmes Memorial Library, Cincinnati General Hospital. Time: 8:15 p. m., third Monday of each month except June, July and August.

Cleveland Academy of Medicine, Section of Ophthalmology and Otolaryngology

Chairman: Dr. A. D. Ruedemann, 2020 E. 93d St., Cleveland.
Secretary: Dr. Fred W. Dixon, 1029 Rose Bldg., Cleveland.
Place: Winton Hotel. Time: Fourth Friday of each month.

Cleveland Ophthalmological Club

Chairman: Dr. A. B. Bruner, 629 Euclid Ave., Cleveland.
Secretary: Dr. M. W. Jacoby, Hanna Bldg., Cleveland.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. John Milton Griscom, 2213 Walnut St., Philadelphia.
Clerk: Dr. Alexander G. Fewell, 1924 Pine St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. F. W. Thomas, 327 E. State St., Columbus, Ohio.
Secretary-Treasurer: Dr. H. D. Emswiler, 370 E. Town St., Columbus, Ohio.
Place: Athletic Club. Time: First Monday of each month.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Hugh L. McLaurin, 1719 Pacific Ave., Dallas, Texas.
Secretary: Dr. Maxwell Thomas, 1719 Pacific Ave., Dallas, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. E. G. Linn, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Grace Doane, 614 Bankers Trust Bldg., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month, September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Raymond S. Goux, David Whitney Bldg., Detroit.
Time: 6:30 p. m., first Wednesday of each month.

Eastern New York Eye, Ear, Nose and Throat Association

President: Dr. A. W. Greene, 148 Barrett St., Schenectady.
Secretary-Treasurer: Dr. Joseph L. Holohan, 317 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. T. L. Goodman, 602 W. 10th St., Forth Worth, Texas.
Secretary-Treasurer: Dr. Van D. Rathgeber, 1012 Medical Arts Bldg., Fort Worth.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Grand Rapids Eye, Ear, Nose and Throat Society

President: Dr. Dewey R. Heetderks, 405 Medical Arts Bldg., Grand Rapids, Mich.
Secretary-Treasurer: Dr. Robert G. Laird, 500 Metz Bldg., Grand Rapids, Mich.
Place: Various local hospitals. Time: Third Thursday of alternating months, September to May.

Houston Academy of Medicine, Eye, Ear, Nose and Throat Section

President: Dr. Henry C. Haden, 1914 Travis St., Houston, Texas.
Secretary: Dr. George C. Farrish, 1625 Main St., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Otolaryngological Society

President: Dr. J. C. Daniel, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: University Club. Time: 6:30 p. m., second Thursday of each month from October to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. H. B. Davis, 1101 Grand Ave., Kansas City, Mo.
Secretary: Dr. Byron Black, Professional Bldg., Kansas City, Mo.
Time: Third Thursday of each month from September to May. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. K. C. Brandenburg, 110 Pine Ave., Long Beach, Calif.
Secretary-Treasurer: Dr. Ben K. Parks, 619 Professional Bldg., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Oto-Laryngology

President: Dr. William A. Boyce, 727 W. 7th St., Los Angeles.
Secretary-Treasurer: Dr. John P. Lordan, 2007 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:30 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye, Ear, Nose and Throat Society

President: Dr. J. S. Bumgardner, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. Max Bornstein, Heyburn Bldg., Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. Arthur M. Zinkham, 815 Connecticut Ave., Washington.
Secretary: Dr. E. J. Cummings, 1835 I St., N. W., Washington.
Place: 1718 M St., N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member, in alphabetical order.
Secretary: Dr. R. O. Rychener, 130 Madison Ave., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month.

Milwaukee Oto-Ophthalmic Society

President: Dr. Hilmar G. Martin, 231 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer. Dr. Herbert G. Schmidt, 238 W. Wisconsin Ave., Milwaukee.
Place: University Club. Time: 6 p. m., second Tuesday of each month.

Minneapolis Ophthalmological Society

Chairman: Each member in alphabetical order.
Secretary: Dr. C. W. Rucker, 527 Medical Arts Bldg., Minneapolis.
Place: Hennepin County Medical Society rooms. Time: 6:30 p. m., fourth Monday of each month, October to May, inclusive.

Montgomery County Medical Society

Chairman: Dr. W. J. Blackburn, 663 Reibold Bldg., Dayton, O.
Secretary-Treasurer: Dr. F. J. Driscoll, 986 Reibold Bldg., Dayton, O.
Place: Van Cleve Hotel. Time: 6:30 p. m., bimonthly, first Tuesday from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. Stuart Ramsay, 1496 Mountain St., Montreal, Canada.
Secretary: Dr. J. Rosenbaum, 1396 St. Catherine St., West, Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. Kate S. Zerfoss, 119, 7th Ave., N., Nashville, Tenn.
Secretary-Treasurer: Dr. Fowler Hollabaugh, Doctors Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to June.

New Orleans Ophthalmological and Otolaryngological Society

President: Dr. R. H. Fisher, Chess and Checker Club, New Orleans.
Secretary-Treasurer: Dr. H. F. Brewster, 837 Gravier St., New Orleans.
Place: Eye, Ear, Nose and Throat Hospital. Time: Third Thursday of each month from October to June.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. John H. Dunnington, 30 W. 59th St., New York.
Secretary: Dr. LaGrand H. Hardy, 30 E. 40th St., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. W. H. Stokes, 107 S. 17th St., Omaha.
Secretary-Treasurer: Dr. Delbert K. Judd, 1020 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m., dinner; 7 p. m., program; third Wednesday of each month from October to May.

Passaic-Bergen Ophthalmological Club

President: Dr. E. C. Reynolds, 657 Main Ave., Passaic, N. J.
Secretary-Treasurer: Dr. T. A. Sanfacon, 80 Park Ave., Paterson, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

Chairman: Dr. Sidney L. Olsho, 235 S. 15th St., Philadelphia.
Secretary: Dr. Edmund B. Spaeth, 1930 Chestnut St., Philadelphia.
Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. Glendon E. Curry, Westinghouse Bldg., Pittsburgh.
Secretary: Dr. George H. Shuman, Park Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Pittsburgh Slit Lamp Society

President: Dr. W. W. Blair, 121 University Pl., Pittsburgh.
Secretary: Dr. George H. Shuman, Park Bldg., Pittsburgh.
Place: Falk Clinic. Time: 4 p. m., second Friday of every month, except June, July, August and September.

Richmond Ophthalmological and Oto-Laryngological Society

President: Dr. Robert H. Courtney, Professional Bldg., Richmond, Va.
Secretary: Dr. Richard W. Vaughan, Medical Arts Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. R. E. Elliott, 78 S. Fitzhugh St., Rochester, N. Y.
Secretary-Treasurer: Dr. Raphael Farber, 280 Monroe Ave., Rochester, N. Y.
Place: Rochester Medical Association, 113 Prince St. Time: 8 p. m., third Monday of each month from October to May.

St. Louis Ophthalmic Society

President: Dr. Carl T. Eber, 308 N. 6th St., St. Louis.
Secretary: Dr. W. M. James, 508 N. Grand Ave., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

San Antonio Ophthalmolo-Oto-Laryngological Society

President: Dr. Oscar H. Judkins, 414 Navarro St., San Antonio, Texas.
Secretary-Treasurer: Dr. Wilfred E. Muldoon, 414 Navarro St., San Antonio, Texas.
Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Lewis F. Morrison, 490 Post St., San Francisco.
Secretary: Dr. Joseph W. Crawford, 490 Post St., San Francisco.
Place: Society's Building, 2180 Washington St., San Francisco.
Time: Fourth Tuesday of every month except May, June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. John T. Crebbin, 624 Travis St., Shreveport, La.
Secretary-Treasurer: Dr. J. A. Wilkinson, Medical Arts Bldg., Shreveport, La.
Place: 1240 Texas Ave. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. C. A. Veasey Jr., 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. Philip B. Greene, Old National Bank Bldg., Spokane, Wash.
Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. W. J. Werfelman Jr., 725 State Tower Bldg., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. Herbert Katz, 212 Medical Arts Bldg., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. Samuel Mortimer Lyon, 122 Bloor St., W., Toronto.
Secretary: Dr. A. Lloyd Morgan, 86 Bloor St., West, Toronto.
Time: First Monday, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. James M. Greear Jr., 1740 M St., N. W., Washington, D. C.
Secretary-Treasurer: Dr. Ernest Sheppard, 927 17th St., Washington, D. C.
Place: Episcopal Eye, Ear and Throat Hospital. Time: 8 p. m., first Monday in November, January, March and May.